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VOLUME 24 NUMBER 1

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JULY 15, 1919

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $6.00

Entered as Second Class Matter, January 23, 1909, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on June 14, 1918.

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PNEUMONIA AND SOME OF ITS COMPLICATIONS AT CAMP BOWIE

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The 2,344 cases of pneumonia and the various complications at the base hospital at Camp Bowie may be grouped into three periods.

Period 1.—From the opening of the base hospital, Sept. 24, 1917, to Jan. 1, 1918: During this period occurred an epidemic of measles, with a large incidence of pneumonia, followed by numerous serious complications and a high death rate.

Period 2.—From Jan. 1, to Sept. 27, 1918: The first three and a half months of this period continued to show a high incidence of pneumonia, though the number and severity of the complications was not as great as in Period 1. From April 15 to September 27 was a comparatively quiet period.

Period 3.—From Sept. 28, 1918, to Jan. 1, 1919: This period included a very high incidence of influenza and a high percentage of pneumonia. In contrast to the pneumonia of 1917, there were comparatively few complications, and these were of a less virulent type.

PERIOD 1

There were 3,624 cases of measles during Period 1* (Chart 1). In addition to the measles there was a widespread infection of the upper respiratory tract throughout the camp. There were 973 cases of pneumonia, and in only 363 of these could we obtain a history of measles within a month preceding the development of the pneumonia. During the epidemic there may have been in camp a number of cases of abortive measles, unrecognized at the time, in which pneumonia developed later.

* Figures given in all charts and tables are as of date of admission, and not of diagnosis or development of complications.

S DB

There were 237 deaths among these pneumonia cases, a mortaiity of 24.4 per cent. (Chart 2). In 17 per cent. of the pneumonia cases empyema developed, with a mortality of 32.5 per cent.

It will be seen from Chart 1 that the first peak was not reached until two weeks after the beginning of the measles epidemic, a much longer time than in the case of the influenza epidemic. There was then a diminution in the number of cases, but following the arrival of 6,000 draft troops, a second peak, almost as great, occurred two weeks after the first. There was a steady decline for ten days thereafter, when the admissions gradually ceased.

The pneumonia curve does not follow that of measles so closely as in the later influenza epidemic. The first pneumonia peak followed the first measles peak by ten days; six days after the second measles peak there was a rise in the number of cases of pneumonia.

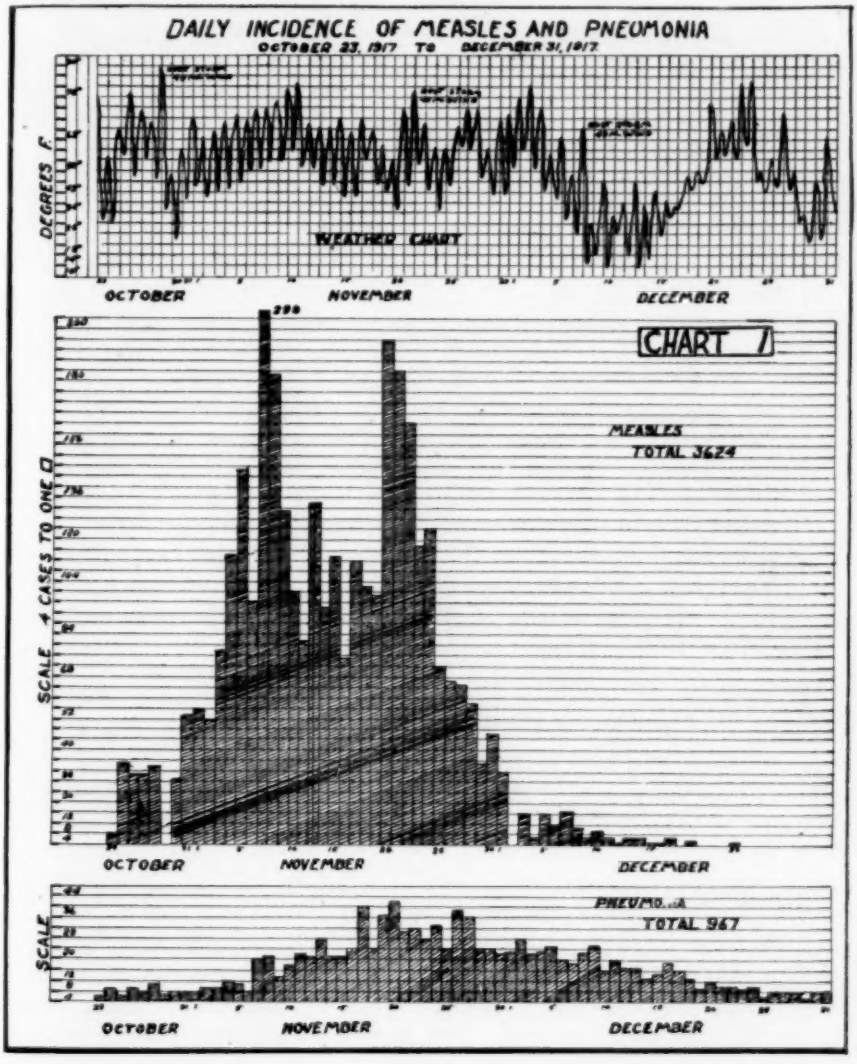
TABLE 1.—Bacteriology of Pneumonia During Period 1 (Dec. 6-15, 1917)

Examinations Made	Organisms Found	No. of Cases	Percentage of Cases
Dec. 6-15, 1917			
Sputum: 62 cases	Pneumococcus Type I	22	35.5
	Pneumococcus Type II	0	0
	Pneumococcus Type II atypical	9	14.5
	Pneumococcus Type III	2	3.2
	Pneumococcus Type IV	29	46.8
Pleural fluids: 17 cases	Hemolytic streptococcus	13	76.0
	Pneumococcus Type II atypical	2	12.0
	Streptococcus viridans	2	12.0
Lung cultures: 30 cases	Hemolytic streptococcus	18	60.0
Postmortem Dec. 15-31, 1917			
Sputum: 33 cases	Pneumococcus Type I	9	27.9
	Pneumococcus Type II	7	21.0
	Pneumococcus Type III	1	3.0
	Pneumococcus Group IV	13	39.0
	Pneumococcus Group IV and Hem. strep.	2	6.0
	Hemolytic streptococcus	1	3.0

Bacteriology.—The bacteriologic data included in this period were furnished by the Red Cross Laboratory Car "Metschnikoff," with Drs. Jobling and Maxwell and Captain Dochez, which was sent to this camp early in December, 1917, to assist the base hospital laboratory, at that time insufficiently equipped and manned to do the necessary work. After Dec. 15, 1917, the base hospital laboratory made routine type determinations by the glucose-blood-broth method (white mice were not available). The results of this work are shown in Table 1. The prevalence of infection with hemolytic streptococci is indicated by its high incidence in the pleural fluids and direct lung cultures.

PERIOD 2

During January and February, 1918, there was a large incidence of pneumonia, the clinical variety showing a greater percentage of lobar pneumonias and differing very little from the variety seen in civil life.


DAILY INCIDENCE OF MEASLES AND PNEUMONIA
OCTOBER 23, 1917 TO DECEMBER 31, 1917
DEGREES F
WEATHER CHART
OCTOBER
NOVEMBER
DECEMBER
CHART 1
MEASLES
TOTAL 3624
SCALE 1 CASES TO ONE
OCTOBER
NOVEMBER
DECEMBER
PNEUMO...A
TOTAL 967
SCALE
OCTOBER
NOVEMBER
DECEMBER

Type I pneumonia constituted 26.5 per cent. of the whole number. Between March 15 and April 15, 1918, 117 cases of pneumonia were admitted to the hospital, 10 of these (8.5 per cent.) showing *Streptococcus hemolyticus* in the sputum. The Type I cases dropped to 13.6 per cent. and Group IV pneumococcus showed 69.2 per cent.

Between March 26 and April 13, 349 cases of an acute respiratory infection were admittted. These were not called "influenza" because of lack of bacteriologic support for such a diagnosis. Clinically, they closely resembled the condition subsequently called influenza, although this diagnosis is questionable.

During the latter half of June, 1918, a large number of recruits in the Detention Camp developed severe bronchitis. Sputum from twenty of the more severe cases was submitted to the laboratory for examination. In addition, nasopharyngeal cultures were made from 60 contacts with these cases and from 60 men, chosen at random, throughout the camp.

Method.—Sputum: The sputum was washed three times in saline and emulsified in broth, then planted in dextrose-blood-broth. After six to eight hours' incubation, human blood-agar plates were streaked from these cultures and were studied after twelve to eighteen hours' incubation, and again after forty-eight hours' incubation. Pneumococcus colonies were fished into dextrose-blood-broth and pure cultures submitted to the test for bile solubility and agglutination with type serums. Colonies showing a wide area of hemolysis and having morphologic characteristics of streptococcus were considered hemolytic streptococcus.

Naso-pharyngeal cultures: The naso-pharynx was swabbed as for meningococcus carrier detection. Swabs were placed immediately into plain broth tubes, and from these, human blood agar plates were streaked and incubated twenty-four to thirty-six hours. Plates were then studied for types of colonies. Organisms such as staphylococci and *Micrococcus catarrhalis* were not recorded. Results are given in Table 2.

TABLE 2.—Organisms Found in Sputum and Nasopharyngeal Cultures from Detention Camp and from Equal Number of Normal Controls (June, 1918)

Organism Present	Sputum		Naso-Pharyngeal			
			Contacts		Controls	
	Cases	Per Cent.	Cases	Per Cent.	Cases	Per Cent.
Hemolytic streptococcus	20	100	..	...	..	...
Pneumococcus Type I	3	15	..	...	..	...
Pneumococcus Group IV	15	75	..	...	..	...
Hemolytic streptococcus, over	..	75	30	50	14	23.3
Pneumococcus undetermined, over	..	75	7	14	2	3.3
Pneumococcus and Hem. streptococcus	..	...	8	13	3	5.0
Neither pneumococci nor streptococci	..	...	20	33	44	75.0

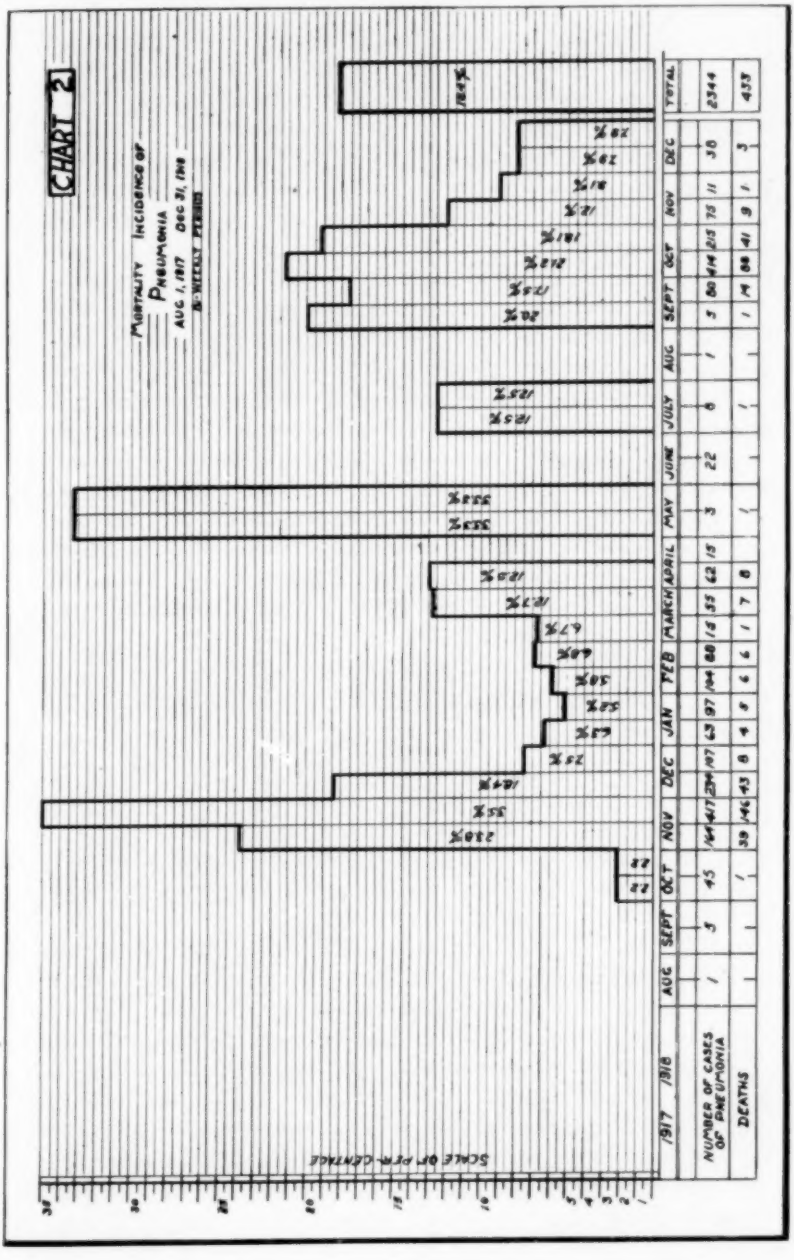


CHART 2
MORTALITY INCIDENCE OF PNEUMONIA
AUG 1, 1917 DEC 31, 1918
BI-WEEKLY PERIODS
SCALE OF PER-CENTAGE
1917 1918
AUG SEPT OCT NOV DEC JAN FEB MARCH APRIL MAY JUNE JULY AUG SEPT OCT NOV DEC TOTAL
NUMBER OF CASES OF PNEUMONIA
DEATHS

During the remainder of Period 2, especially after the Thirty-Sixth Division left in July, there were only forty-three cases of pneumonia with two deaths. Nine of the forty-three showed the hemolytic streptococcus predominating in the sputum, and two were a mixed infection of hemolytic streptococcus and Group IV pneumococcus.

Of the 538 pneumonia patients, only forty-eight gave a history of an antecedent infection within a month. In the great majority of instances there was a definite history of exposure, insufficient clothing, or overheating, followed by injudicious cooling, which may have been the precipitating factor in the onset.

The total mortality for this period was 7.4 per cent., there being forty fatalities among the 538 cases. Fifty-two patients (9.7 per cent.) developed empyema and provided 37.5 per cent. of the total deaths.

Bacteriology.—It is significant that in all the lobar pneumonia cases pneumococci were found in the sputum, and ten of the eighteen fatal cases reacted to specific type serums I and II. Hemolytic streptococci were still an important factor (Table 2), and in three of nine purulent pleurisies this organism was present in addition to the pneumococcus. During the month of April there occurred four cases of interstitial bronchopneumonia caused by the hemolytic streptococcus. These cases occurred at the time of the small epidemic of acute respiratory infection previously described.

PERIOD 3

Influenza. — The development of the epidemic on September 17 began with the admission of cases of a not uncommon type of upper respiratory tract infection, numbering about five daily, before the semblance of an epidemic was evident. On September 26, twenty-four cases of influenza were admitted. During the epidemic which continued to Nov. 15, 1918, 3,876 cases of this infection were admitted to the base hospital. Six hundred and thirty-four cases were held in the observation wards of the Detention Camp.

Blood Counts.—Study of the table of blood counts (Table 3) in uncomplicated influenza shows that during the first five weeks, representing the period of highest incidence, the largest number of counts were below 10,000; the polynuclear percentage was below seventy, and the lymphocyte percentage was over twenty-five. As the severity of the epidemic declined, the total white counts were higher, and the polynuclear percentages were correspondingly increased. The same transition is apparent in the pneumonia following influenza (Table 10), although the percentage of high counts is greater than in the uncomplicated cases.

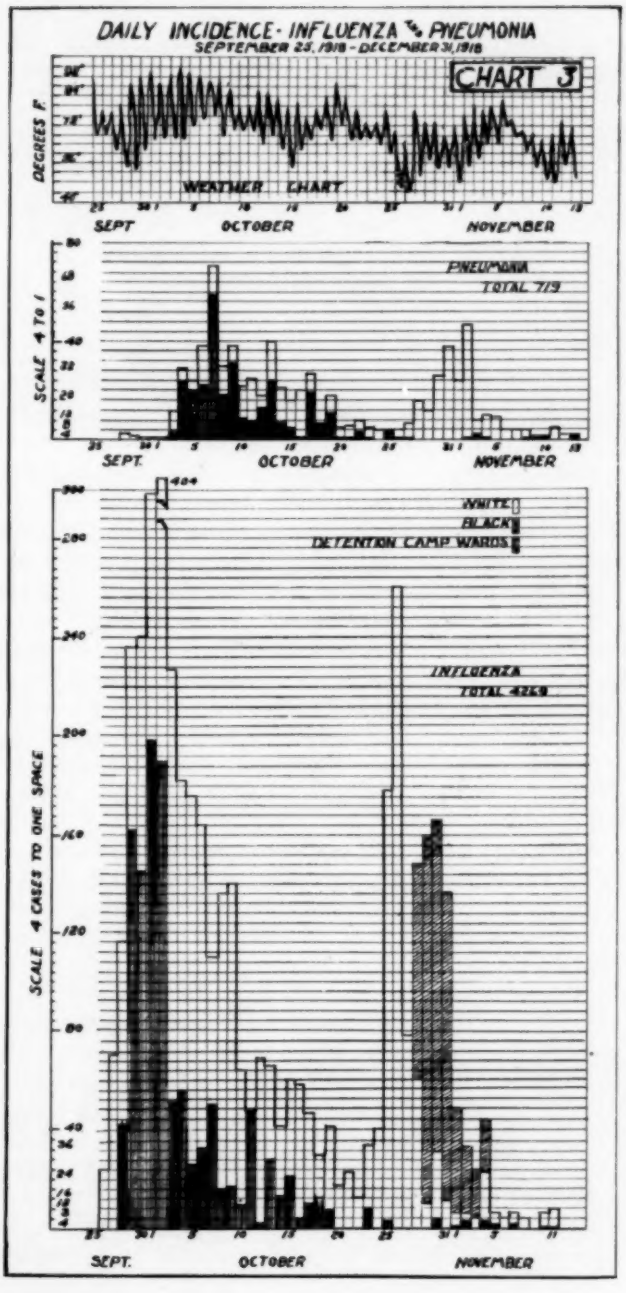

DAILY INCIDENCE - INFLUENZA & PNEUMONIA
SEPTEMBER 23, 1918 - DECEMBER 31, 1918
CHART 3
DEGREES F.
WEATHER CHART
SEPT
OCTOBER
NOVEMBER
SCALE 4 TO 1
PNEUMONIA
TOTAL 719
SEPT.
OCTOBER
NOVEMBER
404
WHITE
BLACK
DETENTION CAMP WARDS
INFLUENZA
TOTAL 4249
SCALE 4 CASES TO ONE SPACE
SEPT.
OCTOBER
NOVEMBER

TABLE 3.—Blood Counts in Uncomplicated Influenza Cases (Based on 400 Counts Made During the First Five Days of the Disease)

	Sept. 25-30, 1918		Oct. 1-31, 1918		Nov. 1-30, 1918	
	Cases	Per Cent.	Cases	Per Cent.	Cases	Per Cent.
Total counts	49	....	212	....	139	....
Under 5,000	...	....	8	3.0	1	1.0
5,000-10,000	37	76.0	138	65.0	33	23.5
Over 10,000	12	24.0	66	32.0	105	75.5
Differential counts	29	....	155	....	126	....
Polymorphonuclear neutrophils						
Under 50 per cent.	1	3.5	3	2.0	...	....
50-70 per cent.	15	51.5	67	43.0	43	34.5
71-85 per cent.	12	41.5	83	53.5	82	65.0
Over 85 per cent.	1	3.5	2	1.5	1	0.5
Lymphocytes						
10-25 per cent.	9	31.0	67	43.5	79	62.5
25-50 per cent.	20	69.0	85	54.5	47	37.5
Over 50 per cent.	...	....	3	2.0	...	....

Leukopenia (counts under 5,000) was not a common finding, though absence of leukocytosis was the rule.

This change in the blood findings was synchronous with a somewhat changed clinical picture. The epidemic reached its peak in numbers in seven days, and at the end of the second week the severity of the infection was decreasing, as shown by a less profound prostration, diminished general malaise, less frequent and milder toxic erythema and more rapid convalescence.

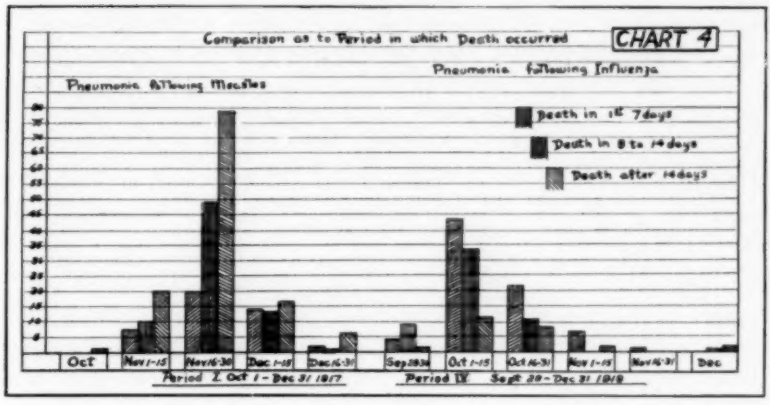
Reference to Chart 3 shows that the first peak of the influenza precedes that of the pneumonia by five days. The second peak, occurring three weeks later, coincident with the arrival of the first increment of drafted troops from Missouri, precedes the second peak of the pneumonia by seven days. There were received at the detention camp during the course of the epidemic 4,108 drafted white men and 2,360 drafted colored men.

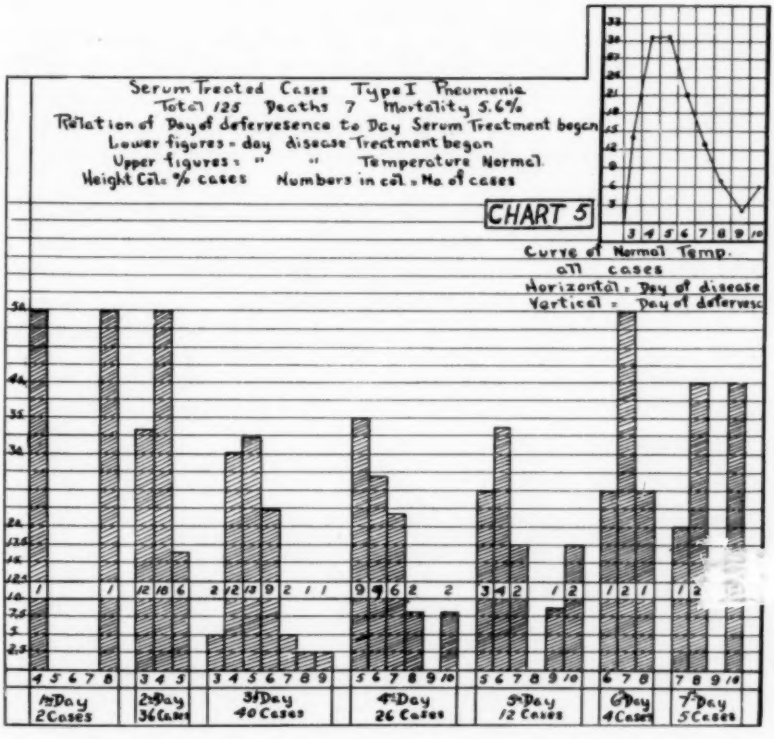
Among the white men, 252 per thousand men who were exposed developed the infection, 114 per thousand developed pneumonia. Not every pneumonia patient gave a history of an antecedent influenza infection. Among the 795 cases of pneumonia, a history of influenza within the preceding month was obtained in 728.

No deaths were attributable to uncomplicated influenza. The total deaths in the 833 cases of pneumonia, numbered 156, a mortality of 18.7 per cent. Thirty-six men (4.3 per cent.) developed empyema and furnished 11.5 per cent. of the total deaths.

It is interesting that in spite of the higher morbidity rate for influenza and pneumonia among black troops, the mortality percentage (17.1 per cent.) among them was somewhat less than that of the white troops (20.8 per cent.).

From Chart 2 it would at first appear that the highest mortality was reached quickly after the onset of the epidemic, the virulence of the infection decreasing thereafter and the mortality diminishing from


Comparison as to Period in which Death occurred
CHART 4
Pneumonia following Measles
Pneumonia following Influenza
Death in 1st 7 days
Death in 8 to 14 days
Death after 14 days
Oct
Nov 1-15
Nov 16-30
Dec 1-15
Dec 16-31
Sep 28-30
Oct 1-15
Oct 16-31
Nov 1-15
Nov 16-31
Dec
Period I. Oct 1 - Dec 31 1917
Period II. Sept 28 - Dec 31 1918


Serum Treated Cases Type I Pneumonia.
Total 125 Deaths 7 Mortality 5.6%
Relation of Day of defervescence to Day Serum Treatment began
Lower figures = day disease Treatment began
Upper figures = " " Temperature Normal
Height Col = % cases Numbers in col = No of cases
CHART 5
Curve of Normal Temp.
all cases
Horizontal = Day of disease
Vertical = Day of defervesc
1st Day 2 Cases
2d Day 36 Cases
3d Day 40 Cases
4th Day 26 Cases
5th Day 12 Cases
6th Day 4 Cases
7th Day 5 Cases

21.2 and 19.1 per cent. to 12 and 9.1 per cent., respectively, for semimonthly periods. That this may have been partly true is evidenced by the fact that the patients admitted after the first two weeks did not appear to be so severely ill. That the virulence of the infecting organism persisted is shown by the incidence and mortality of pneumonia among the Missouri drafted men, who arrived three weeks after the peak of the epidemic was reached. These men arrived in camp from October 22 to October 25. They were overtaken by influenza October 23-31 and developed pneumonia October 28 to November 4. Among them there developed 199 cases of pneumonia with thirty-nine deaths, a mortality (19.6 per cent.) almost equal to that occurring at the height of the epidemic. The lower total mortality for the first half of November was due to the inclusion of ninety-one scattered cases occurring among troops that had been in camp longer. Among these cases there were only eleven deaths, a mortality of 12 per cent.

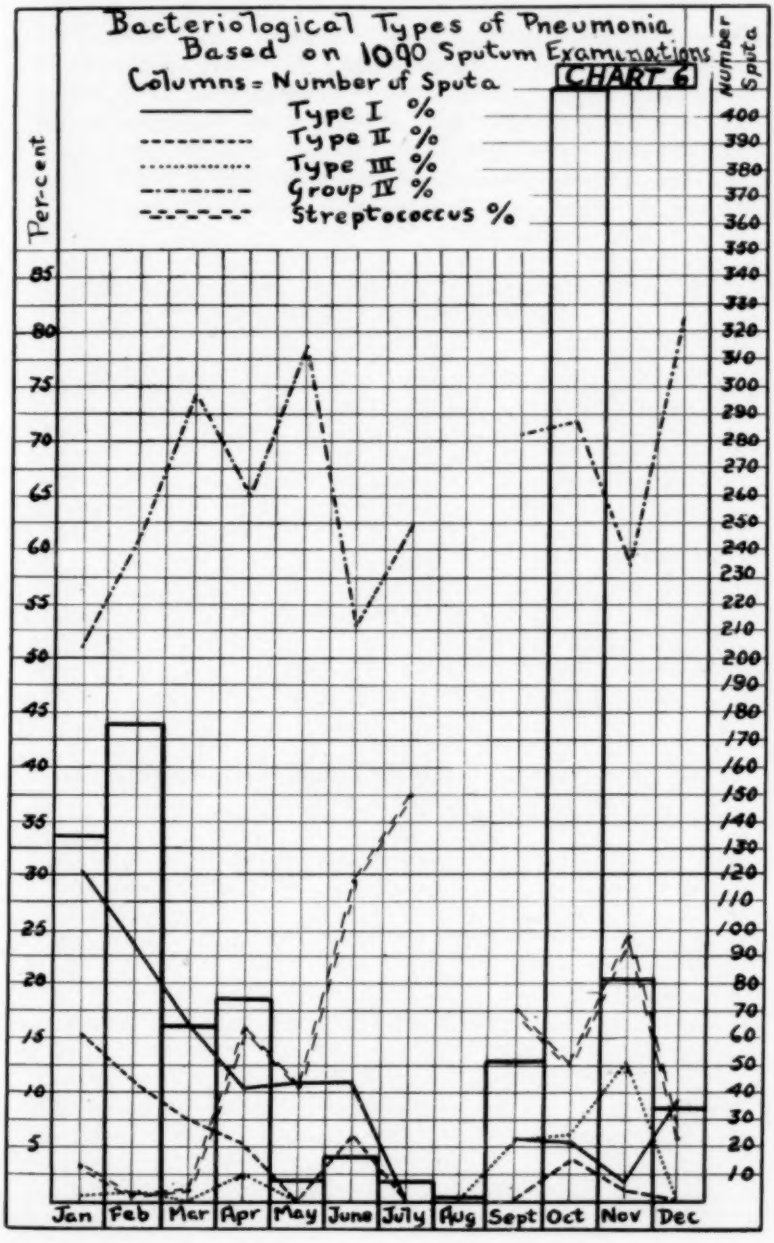
Bacteriology.—Sept. 25, 1918, routine naso-pharyngeal swabs were made in all cases admitted with the diagnosis of influenza. In all, seventy-five cases were examined satisfactorily.

Method: Swabs were made from the naso-pharynx as described in "Standard Method for Meningococcus Carriers for U. S. Army." These were first streaked on human blood-agar plates, and afterward immersed in glucose-blood-broth. The latter cultures were incubated about six hours and human blood-agar plates were then streaked from them.

Identification: Streptococci and pneumococci by "Standard Method for U. S. Army," except that press of other work prevented identification of types of pneumococci. Plates were incubated eighteen to twenty-four hours. Influenza bacilli when found in quantity were present in characteristic growth in this time. The results are shown in Table 4.

TABLE 4.—Bacteriology of Naso-Pharyngeal Cultures in Influenza

	Number	Per Cent.
Hemolytic streptococci (colonies over 75 per cent.)	34	45
Associated organisms:		
Pneumococci (type undetermined)	18	
Staphylococci	19	
Unidentified Gram positive bacilli	3	
Pneumococci, type undetermined (colonies over 75 per cent.)	26	35
Associated organisms:		
Hemolytic streptococci	7	
Nonhemolytic streptococci	2	
Staphylococci	11	
Micrococcus catarrhalis	1	
Influenza bacilli present	7	9
Associated organisms:		
Hemolytic streptococci	3	
Pneumococci (type undetermined)	2	
Micrococcus catarrhalis	2	
Staphylococci	4	
Nonhemolytic streptococci (colonies over 75 per cent.)	8	10
Associated organisms:		
Staphylococci	6	
Micrococcus catarrhalis	2	
Friedländer bacilli	1	


Bacteriological Types of Pneumonia
Based on 1090 Sputum Examinations
Columns = Number of Sputa
CHART 6
Type I %
Type II %
Type III %
Group IV %
Streptococcus %
Per-cent
Number Sputa
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
400
390
380
370
360
350
340
330
320
310
300
290
280
270
260
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Jan
Feb
Mar
Apr
May
June
July
Aug
Sept
Oct
Nov
Dec

Postmortem Bacteriology: The bacteriology during Period 3, as determined by lung cultures and the incidence of complications in the three types of cases, (1) lobar pneumonia, (2) bronchopneumonia of the confluent lobular type, and (3) bronchopneumonia of the interstitial type, is shown in Tables 5, 6 and 7. The group showing the interstitial type of pneumonia and the highest proportion of complications, showed hemolytic streptococcus in 64 per cent. of lung cultures, just as our experience with streptococcus pneumonia complicating measles had led us to expect.

TABLE 5.—Bacteriology of Lobar Pneumonia (Twenty-Four Cases) as Determined by Lung Cultures

	Cases
Not examined	8
Pneumococcus, Type II, alone	1
Pneumococcus, Group IV, alone	7
Pneumococcus, Group IV and influenza	2
Pneumococcus, Group IV, influenza and nonhemolytic streptococcus	1
Pneumococcus, type undetermined, alone	3
Pneumococcus, type undetermined and influenza	1
Pneumococcus, type undetermined and Micrococcus catarrhalis	1
Influenza bacillus, 4 cases; 25 per cent.	
Complications	Per Cent.
Pleurisy, purulent	12.5
Pleurisy, fibrinous	30.0
Pleurisy, serofibrinous	12.5
Pleurisy, serous	8.0
Meningitis, purulent	12.5
Substernal pus pocket	4.0
Lung abscess	4.0
Peritonitis, purulent	4.0
Edema, brain	4.0
Average duration of disease 9.2 days.	

TABLE 6.—Bacteriology of Bronchopneumonia—Confluent Lobular Type (68 Cases)

	Cases
Not examined	17
Pneumococcus, type undetermined, alone	10
Pneumococcus, type undetermined and influenza	5
Pneumococcus, type undetermined and Micrococcus catarrhalis	1
Pneumococcus, Group IV, alone	14
Pneumococcus, Group IV and influenza	1
Pneumococcus, Type III, alone	1
Pneumococcus, Type I, alone	2
Influenza and M. catarrhalis	1
Hemolytic streptococcus, alone	2
Hemolytic streptococcus and pneumococcus, Group IV	1
Nonhemolytic streptococcus, alone	11
Nonhemolytic streptococcus and influenza	1
Bacillus of Friedländer, alone	1
Hemolytic streptococcus, 3 cases; 6 per cent.	
Influenza bacillus, 8 cases; 16 per cent.	
Complications	Per Cent.
Pleurisy, purulent	4.5
Pleurisy, serofibrinous	11.0
Pleurisy, fibrinous	23.0
Pleurisy, serous	4.5
Pericarditis, serofibrinous and purulent	3.0
Metastatic abscess	3.0
Average duration of disease 8.5 days.	

Influenza bacilli were found in 16 per cent. of the remaining bronchopneumonias and in 25 per cent. of the lobar pneumonias, and always associated with other organisms.

In all of the lobar pneumonia cases the pneumococcus was found. In the bronchopneumonia cases of the confluent lobular type, thirty-five (70 per cent.) yielded pneumococcus Group IV pneumococcus, type undetermined, or nonhemolytic streptococcus.

Satisfactory cultures were made postmortem from heart's blood in eighty-one cases, with results as shown in Table 8.

TABLE 7.—BACTERIOLOGY OF BRONCHOPNEUMONIA—INTERSTITIAL TYPE (33 CASES)

	Cases
Not examined	11
Streptococcus, hemolytic alone	10
Streptococcus, hemolytic and pneumococcus, Group IV	1
Streptococcus, hemolytic and pneumococcus, undetermined	2
Streptococcus, hemolytic and influenza	1
Streptococcus, nonhemolytic, alone	1
Streptococcus, nonhemolytic and influenza	1
Pneumococcus, undetermined, alone	1
Pneumococcus, undetermined and Friedländer bacillus	1
Pneumococcus, Type III, alone	1
Pneumococcus, Group IV, alone	3

Streptococcus, hemolytic, 14 cases; 64 per cent.
Influenza bacillus, 2 cases: 9 per cent.

Complications	Per Cent.
Pleurisy, purulent	40
Pleurisy, serofibrinous	18
Pleurisy, fibrinous	28
Pericarditis, serofibrinous and purulent	9
Peritonitis, purulent	9
Substernal pus pocket	9
Metastatic abscess	3
Lung abscess	6

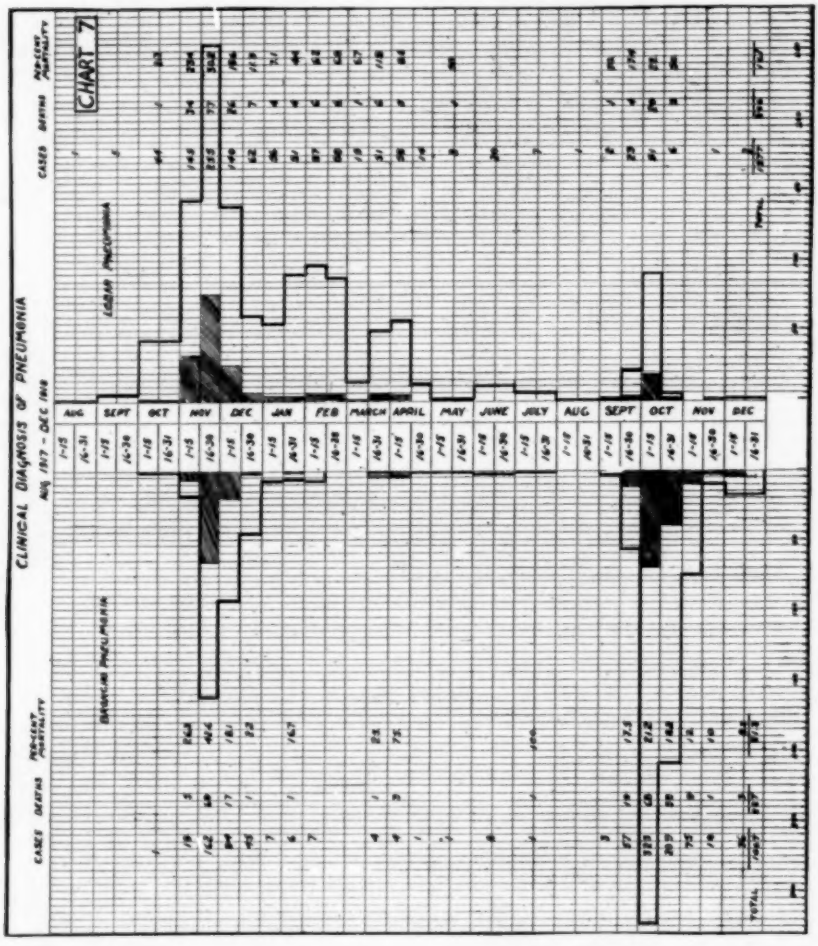
Average duration of disease 14.5 days.

TABLE 8.—BACTERIOLOGY OF CULTURES FROM HEART'S BLOOD (POSTMORTEM)

Total cultures	81
No growth	19
Pneumococcus, type undetermined	19
Pneumococcus, Group IV	17
Pneumococcus, Type I	1
Pneumococcus, Type II	2
Pneumococcus, Type III	1
Streptococcus, hemolytic	11
Streptococcus, nonhemolytic	11

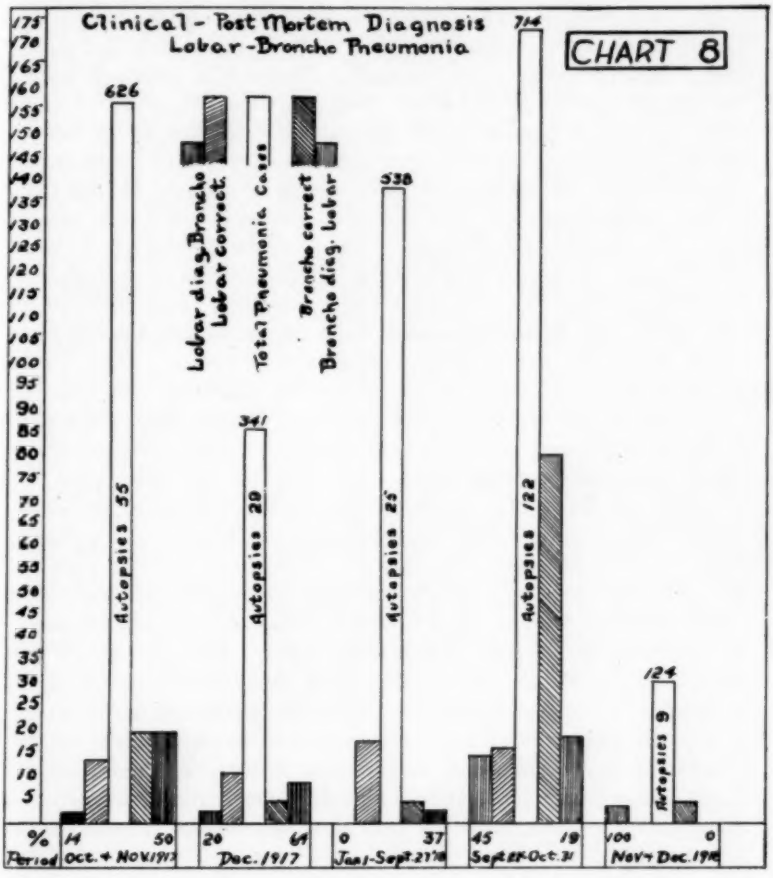
Diagnosis.—Certain cases, especially cases of lobar pneumonia, have offered no difficulty in diagnosis. In the secondary pneumonias, those following measles in 1917, and especially those following influenza in 1918, it was the rule rather than the exception for the signs to be so irregular as to offer the greatest difficulty in diagnosis, not only as to the evidence of consolidation, but especially as to the clinical variety. The sputums from these cases have practically all shown streptococcus, pneumococcus Group IV, or a mixed infection.

How badly we have failed in the differentiation of the clinical types of pneumonia under the conditions existing here, may be seen by reference to Chart 8.



In October and November, 1917, during the measles epidemic, there were 626 cases of pneumonia, of which fifty-five came to necropsy. Among these fifty-five cases, lobar pneumonia was diagnosed correctly in fourteen, as bronchopneumonia in two (14 per cent.). Bronchopneumonia was diagnosed correctly in twenty cases, as lobar pneumonia in twenty cases (50 per cent.).

In September and October, 1918, during the influenza epidemic, there were 714 cases of pneumonia, of which 122 came to necropsy. Of these 122 cases, eighteen were diagnosed correctly lobar pneumonia, fifteen were wrongly called bronchopneumonia (45 per cent.). Eighty-one cases were properly diagnosed as bronchopneumonia; nine-



teen cases were wrongly called lobar pneumonia .(19 per cent.). There were certain extenuating circumstances for these wrong diagnoses. Even at the postmortem table the differentiation was frequently puzzling. The fact remains that statistics based on clinical differentiation between lobar and bronchopneumonia seen at this hospital during the first sixteen months of its existence are not reliable. For this

reason we have not included the differentiation in the tables and charts, except in Chart 7, which will serve as a comparison with figures furnished from other sources.

Onset.—As this was observed in the pneumonias following measles and in those following influenza, there was a great difference in the two epidemics. In 1917 it apparently took longer for an acute infection of the upper respiratory tract to develop into a pneumonia. A history of an acute infection existing several weeks before the pneumonia developed was often obtained. In the post-influenzal pneumonias, the signs of consolidation rarely appeared later than five days after the initial symptoms of the influenza; the duration of the febrile period of influenza having been two to five days, most often three. The infections following both epidemics were usually of the descending type. In some cases the involvement of the lungs and pleura appeared almost simultaneously, leaving it doubtful whether the consolidation or the empyema came first. In 1917, especially, the pleural involvement was often the initial and outstanding feature; the pain was intense, the prostration extreme, the face flushed, the features drawn and fluid (usually streptococcal) formed before signs of consolidation were manifest. In the majority of cases pain and chill did not figure in the onset. The increased temperature, high pulse and increased respiratory rate were indications for careful and frequently repeated physical examinations.

During periods 1 and 2 cases were seen occasionally in which the signs of meningitis ushered in the infection. Usually, the meningeal signs persisted for about twenty-four hours; then the first signs of consolidation would appear. Spinal fluids were negative.

Signs.—The physical signs in the majority of these difficult cases were extremely irregular and rarely frank. Dulness, suppressed breath sounds, often moist crackling râles, especially at the height of inspiration, or even a change in the quality of the breath and voice sounds—one or more of these, but rarely all, were the bases of the diagnosis. In the absence of supporting evidence—such as the subsequent course of the disease, leukocyte counts and roentgenograms—many of these cases would not have been diagnosed. It was not an infrequent experience to have the frank signs follow several days after the decline of temperature and improvement in the general condition.

Lobes Involved.—Of 1,533 cases in which the first involvement noted affected only one lobe, the right lower lobe was involved first in 711 cases, the left lower lobe in 679 cases, the right upper lobe in 54 cases, the left upper lobe in 48 cases, and the right middle lobe in 41 cases. In a large number of the cases of pneumonia associated with

the influenza epidemic, the initial involvement was simultaneous in both lower lobes. It is of anatomic interest to note that in four necropsies an additional lobe was observed twice on the left and twice on the right side.

Blood Counts.—In Periods 1 and 2 the blood counts were such as are ordinarily encountered in pneumonia. During the first five days of the disease about 85 per cent. of the total number of white counts made was over 10,000, and in the same proportion of cases the polynuclear percentage was 70 or over (Table 9).

TABLE 9.—BLOOD COUNTS IN PNEUMONIA

	Period 1 Sept. 23-Dec. 31,		Period 2 Jan. 1-Sept. 27,		Period 2—Following Influenza					
					Sept. 28-30,		Oct. 1-31,		Nov. 1-30,	
	Cases	Per Cent.	Cases	Per Cent.	Cases	Per Cent.	Cases	Per Cent.	Cases	Per Cent.
Total Counts:										
During first five days—										
Under 5,000	1	2	2	4	3	10	10	8	..	..
5,000-10,000	4	8	6	12	12	38	79	60	7	30
Over 10,000	45	90	43	84	16	51	41	31	16	70
After five days—										
5,000-10,000	4	19	1	14	6	43	24	30	..	..
Over 10,000	18	81	6	86	8	57	57	70	3	100
	72		58		45		211		26	
Differential Counts:										
Polymorphonuclears—										
50-70 per cent.	7	10	2	5	6	25	42	43	2	8
70-85 per cent.	43	64	24	53	17	75	53	54	19	83
Over 85 per cent.	17	25	19	42	..	..	3	3	2	8
	67		45		23		98		23	

When the figures for these two periods are compared with those for Period 3, it will be noted that they are very nearly reversed—60 per cent. of these counts being *under* 10,000, while in 35 per cent. the polynuclear percentage was below seventy.

It is not unreasonable to infer that the failure of the individual to react to his pneumonia with a leukocytosis at this time is evidence of a diminished resistance produced by the preceding influenza. In this connection it is interesting to note that of thirty-one counts made in cases in which no antecedent history of influenza was present during Period 3, twenty-seven were over 10,000 (average 15,000) and only four were below 10,000. Also that the average duration of illness in fatal cases during the first two periods was twenty-one days, while in the last period it was eleven days.

Blood Cultures.—Of 254 satisfactory blood cultures taken during life, thirty-five, or 13.8 per cent. were positive. Of the 219 cases in which sterile blood cultures were obtained, twenty-four, or 11 per cent., of the patients died, whereas of the thirty-five cases with positive blood

cultures fourteen patients, or 40 per cent., died. This is in accord with the view that a positive blood culture during life makes the prognosis grave.

Bacteriological Examination of Sputum. — Chart 6 shows type determinations for the year 1918. Of the 1,371 cases of pneumonia occurring in 1918, the sputum in 1,090, or 79.5 per cent., was typed. From Dec. 28, 1917, to Jan. 20, 1918, Type III serum was not obtainable; therefore, Group IV for this period may include some Type III cases. During the four winter months—December, January, February and March—the percentage of incidence of Type I was 23.8. The incidence during the period of good weather was 5.9 per cent. With Type II the winter months showed an incidence of 11.1 per cent. — the summer months 3.1 per cent. In contrast to the decreased incidence of these fixed types, Group IV pneumococcus shows 61.9 per cent. in the winter months and 69.2 per cent. in the summer months. The streptococcus curve includes both hemolytic and non-hemolytic streptococci, and resembles the Group IV curve in its variations.

TABLE 10.—Pneumonia: Cases and Mortality on the Basis of 1,090 Sputum Type Determinations

	Cases	Deaths	Mortality, per Cent.
Pneumococcus Type I	142	7	4.9
Pneumococcus Type II	68	14	20.6
Pneumococcus Type III	45	6	13.3
Pneumococcus Group IV	722	75	10.4
Pneumococcus Group IV and Hemolytic strep.	25	6	24.0
Nonhemolytic streptococcus	5	5	100.0
Hemolytic streptococcus	83	11	13.3

The mortality in the various types of infecting organisms, as determined by sputum examinations, is shown in Tables 10 and 11. It is interesting to note the variations in mortality for the same type in different periods. All types, with the exception of Type III, showed a much higher mortality during Period 3 (accompanying the influenza epidemic) than they had shown during the first nine months of the year.

TABLE 11.—Periods 2 and 3. Mortality of Various Types of Organisms Compared

	Mortality Percentage, Jan.-Sept.	Mortality Percentage, Oct.-Dec.
Pneumococcus Type I	4.3	7.4
Pneumococcus Type II	15.0	37.5
Pneumococcus Type III	20.0	12.5
Pneumococcus Group IV	7.6	12.0
Streptococcus—hemolytic and nonhemolytic	7.4	23.0

Experience at this hospital has shown that to limit the investigation of sputum to a determination of the type of pneumococcus present,

does not always give a reliable guide as to the nature of the existing infection. We need only call attention to a comparison of our sputum type determination, with the bacteriology found in pleural fluids and at necropsy, during Period 1 (Table 1) to illustrate this point. It seems necessary to attempt to determine the predominating organisms. Our practice has been to estimate this from a differential count of colonies on human blood-agar plate streaked from either first culture in glucose-blood-broth or from the peritoneal cavity of the mouse.

Comparing the findings in the sputum with the other bacteriologic findings in the same case, such as from the examination of blood cultures, pleural fluids, lung cultures, necropsy, etc., should furnish the best evidence as to their value in ordinary hospital practice. Such a comparison is made in Table 12. The percentage of correspondence is high, taking into consideration the conditions under which the work was done, and indicate that this procedure should remain one of our routine diagnostic methods for the study of pneumonia.

TABLE 12.—Comparison of Sputum with Other Bacteriologic Findings

Sputum	With Other Bacteriologic Findings	Corresponding	Per Cent.	Different	Per Cent.
Pneumococcus Type I	7	5	71	2	29
Pneumococcus Type II	12	6	50	6	50
Pneumococcus Type III	6	1	16	5	84
Pneumococcus Group IV	74	40	54	34	46
Streptococcus, hemolytic	17	13	76	4	24
Streptococcus, nonhemolytic	4	3	75	1	25

Course.—The progression toward a fatal termination varied considerably in those cases occurring in the fall of 1917, as contrasted with those in the fall of 1918. In the former period an extreme cyanosis, hoarse, barking cough, anxious facies, with all the accessory muscles of respiration in use, presented a fearful picture of what seemed the horror of death. In 1918, there was comparatively little of this. Even in the streptococcus infections death was preceded by a much more quiet period. This was especially true in the case of the negroes (there were none in camp in 1917). They usually remained quiet with shallow respirations, and met death quietly.

Chart 4 shows the deaths occurring in the two epidemic periods with reference to the duration of the illness. Accompanying the measles epidemic it is always an increasing number for the first week, the second week and after the second week. During the influenza epidemic the number dying in the first week is greater than that in the second week, and the least number survive more than 14 days.

TREATMENT OF PNEUMONIA

Serum Therapy.—The specific serum has been used in all Type I cases, except those which had practically defervesced at the time of type determination.

The time between sending the sputum to the laboratory and the giving of the serum was eight to twelve hours, except during the epidemic, when the stress of work prevented the desensitizing of all pneumonia patients as soon as the diagnosis was made.

There were during 1918, 142 Type I infections. One hundred and twenty-five patients were treated with serum; seven died — a mortality of 5.6 per cent. (Table 13). Four of these seven deaths, while charged to pneumonia, really were caused by empyema, twenty-nine, twenty-eight, twenty-four and fifteen days, respectively, after the development of the pneumonia. Eliminating these deaths, the mortality of the treated cases would be 2.4 per cent.

TABLE 13.—COMPLICATIONS

	Total Cases	Cases Recognized Only at Necropsy	Per Cent. Recognized Only at Necropsy
Empyema	249	28	11
Pleurisy with effusion	101	38	38
Otitis media—suppurative (22 bilateral)	105		
Otitis media—catarrhal (13 bilateral)	40		
Mastoiditis (2 bilateral)	25	3	12
Pericarditis	24	15	58
Metastatic abscess	17	3	18
Emphysema, subcutaneous, generalized	8		
Emphysema, mediastinal tissues only	10	10	100
Lung abscess	9	6	67
Meningitis	12	2	17
Peritonitis	12	8	67
Substernal pus pockets	7	7	100
Thrombophlebitis	8		
Nephritis, chronic parenchymatous	1		
Nephritis, acute toxic	18	18	100
Sinusitis	5		
Myocarditis	1		
Toxic psychosis	1		

Seventeen Type I infections were untreated. None of these patients died. The untreated patients were for the most part those who, because of the mildness of their infection, or delay in being sent into the hospital, had their crisis before the type of the infection could be determined. A few of these patients were sensitive to horse serum, but were not treated because they were not very sick.

No serious results have followed the administration of serum, and we feel that our experience is a strong argument for its use. The earlier it is used, the more striking are the results obtained. This is shown in Chart 5, which gives the relation of the day of defervescence to the day on which serum treatment was begun.

Digitalis.—All patients received digitalis in large doses as soon as the diagnosis was made. In Period 3, when a standardized tincture was obtained, it was administered in therapeutic dosage.

General Measures.—Treatment other than that already referred to was symptomatic.

Gross Pathology.—Period 1: The first cases coming to necropsy in November, 1917, showed the well known, typical lesions of acute lobar pneumonia. Of the first eight cases two showed pleural effusions — one serofibrinous and the other purulent.

TABLE 14.—Relation of Pleural Exudate and Sputum in Sixty-Eight Cases of Empyema

	Cases	Deaths	Percentage of Mortality
1. Pneumococcus in both sputum and pleural fluid	32	6	19
2. Hemolytic streptococcus in both sputum and pleural exudate	3	1	33
3. Pneumococcus and hemolytic streptococcus in both sputum and pleural exudate	30	10	33
4. Sterile empyemas, pneumococcus in sputum	3	0	0
Total	68	17	25

As measles became more prevalent, and as both the incidence and mortality of pneumonia rose, the picture changed. More lobes were involved. Instead of feeling uniformly firm and airless, the affected tissue felt nodular, or "shotty," and distinct crepitation could be elicited between the firm nodules. Fibrinous deposits over the pleural surface were more constant and more extensive. On section, the cut surface of lung presented a mottled appearance, usually a dark, bluish-red background, with many small slightly elevated grayish red areas, each presenting the opening of a bronchiole, at or near its center. In many cases these areas were confluent. The interlobular septums were distinctly visible, dividing the lobe into a number of irregularly shaped areas. Abscess formation, especially multiple small abscesses, was occasionally found.

Effusions into the pleural cavity became increasingly frequent, and were usually purulent. Adhesions between the visceral and parietal pleura occurred, often dividing the pleural cavity into two or more distinct compartments. Perhaps, the most frequent site of such adhesion was between the anterior edge of the lung and the costal margin, the inner surface of the sternum or pericardial sac. Here elongated pockets were formed, at times divided by transverse bands into two, which contained thick greenish pus and masses of fibrin. Adhesions between the lobes with formation of interlobular abscesses were also found.

The pericardium was involved in many cases. In some instances only the external surface showed a fibrin deposit of varying thickness with organization, and adhesion to sternum, ribs and left lung. In other instances, the inner surface was dull, covered with a rough fibrin deposit, and the sac contained a large amount of serofibrinous or purulent fluid, in which hemolytic streptococci were found.

TABLE 15.—PROCEDURE IN EMPYEMA

Method of Treatment	Aspiration No.	Period 1		Period 2		Period 3		Total Cases	Mortality per Cent.
		Cases	Deaths	Cases	Deaths	Cases	Deaths		
Aspiration alone	1	21	20	..	..	2	2	23	84
	2	4	3	1	1	2	1	7	71
	3	3	2	1	1	1	0	4	75
	8	..	..	..	..	1	0	1	0
Costatectomy preceded by aspiration	1	89	26	27	5	5	1	121	26
	2	10	2	8	0	2	0	20	10
	3	4	0	6	1	..	..	10	10
	4	2	1	1	0	1	0	4	0
	5	..	..	..	..	1	0	1	0
	7	1	1	..	..	1	0	2	0
	9	..	..	1	0	..	..	1	0
	10	..	..	..	..	1	0	1	22
Thoracotomy preceded by aspiration	1	11	7	..	..	1	0	12	58
	2	3	3	..	..	2	0	5	60
	3	1	1	1	1	2	1	4	75
	4	..	..	..	..	1	1	1	100
	5	..	..	..	..	1	1	1	100

SUMMARY

	Costatectomy			Thoracotomy			Aspiration			Total		
	Cases	Deaths	Mortality per Cent.	Cases	Deaths	Mortality per Cent.	Cases	Deaths	Mortality per Cent.	Cases	Deaths	Mortality per Cent.
Period 1* Oct. 1-Dec. 31, 1917	106	30	28.3	15	11	73	29	26	89	150	67	44 6
Period 2 Jan. 1-Sept. 27, 1918	43	6	14.0	7	1	100	3	3	100	47	10	21.3
Period 3 Sept. 27-Dec. 31, 1918	11	1	9.0	1	3	43	6	2	33	24	6	25.0
Total	160	37	....	23	15	....	38	31	....	221	83	37.5

* Two cases (2 deaths) included in totals for aspiration only had no aspiration before death.

Microscopic. — The microscopic picture in these cases was that described by MacCallum[1] as interstitial pneumonia. The illustrations

1. Cole R., and MacCallum, W. G.: Pneumonia at a Base Hospital, J. A. M. A. **70**:1147, 1918.

show some of the constant findings — peribronchial consolidation, involvement of interstitial tissue, and extensive fibrino-purulent pleurisy.

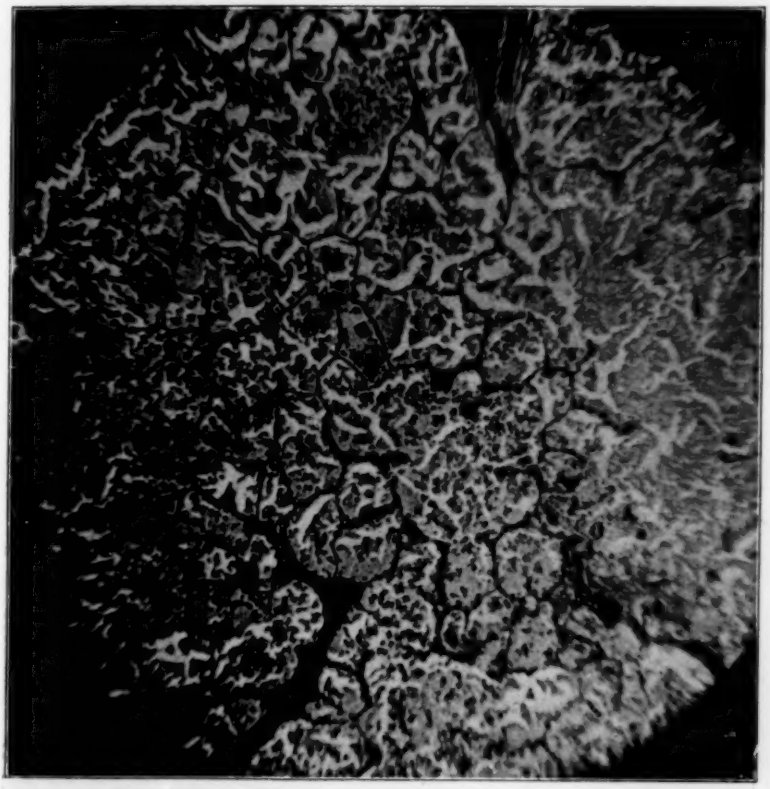


Fig. 1.—Section of lung affected with a confluent lobular bronchopneumonia following influenza. Early exudate.

PERICD 2

Of twenty-five postmortems, lobar pneumonia was found in nineteen cases; bronchopneumonia, of the interstitial type, was found in six cases. The incidence of purulent pleurisy was high (50 per cent.). This may be explained by the fact that five of the six bronchopneumonia cases showed this complication, and hemolytic streptococci were found as complicating organisms in one-third of the cases following pneumococcus infection.

PERIOD 3

Gross Pathology.—Three distinct types of cases were found: (1) lobar pneumonia; (2) bronchopneumonia of interstitial type, the lesions of which have just been described, and (3) bronchopneumonia of a lobular or confluent type.

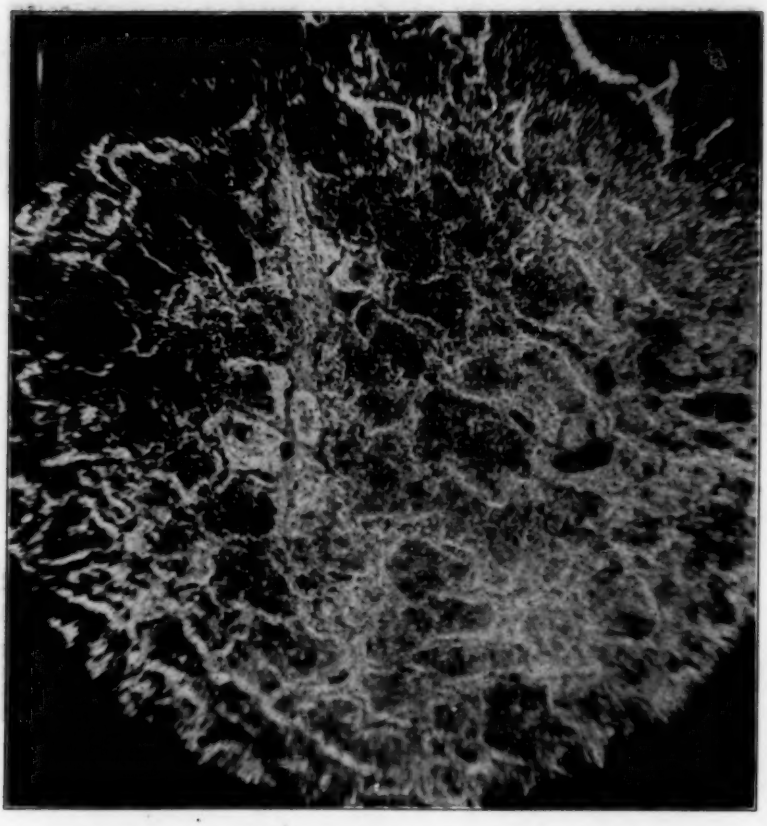


Fig. 2.—Section of lung affected with a confluent lobular bronchopneumonia following influenza. Later exudate.

In the latter cases, the lungs were large, moderately firm, all more or less nodular. Frequently, by careful palpation, crepitating areas could be felt, even in a lobe which was apparently completely consolidated. The pleural covering was usually smooth and transparent, many cases showing scattered small areas of subpleural hemorrhage. Fine fibrinous deposits were found in some cases very early in the course of the

pneumonia. In those cases which showed emphysema of the mediastinal tissues there was usually an emphysema just beneath the pleura which extended mainly along the interlobular septa.

Section of the lung was followed by the outpouring of a large amount of dark, bloody fluid. The cut surface was dark, bluish red, mottled with lighter areas, which varied in color from a deep brownish-

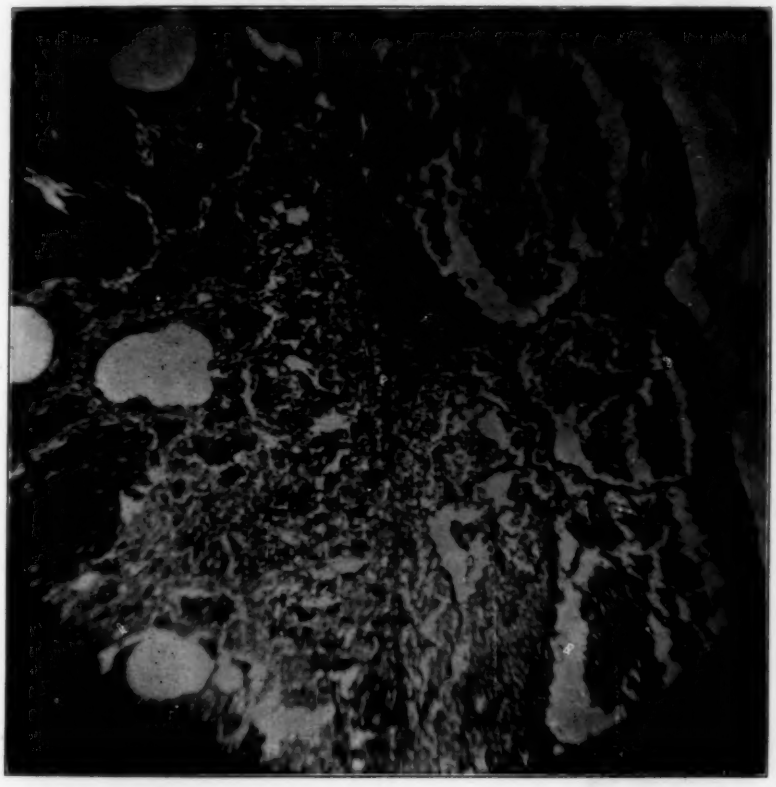


Fig. 3.—Section of lung showing a pleural lesion in a case of interstitial pneumonia caused by the hemolytic streptococcus.

red to a light grayish-red, or grayish-yellow, and varied in size from one or two centimeters in diameter up. It was very common to find areas of different color and consistency in the same lobe. In the lower lobes these areas were largest and most confluent, so that at times it was difficult to say whether or not the consolidation was homogeneous. In such cases, however, the upper lobes always showed distinct patchy consolidation.

The microscopic picture is shown in the accompanying illustrations. Its characteristic features were the intense edema and congestion of all interstitial tissues, the marked predominance of bloody exudate in the alveoli in most cases, and the irregular distribution of the lesion, not strictly peribronchial nor diffuse, but showing areas at different stages of development in the same section.

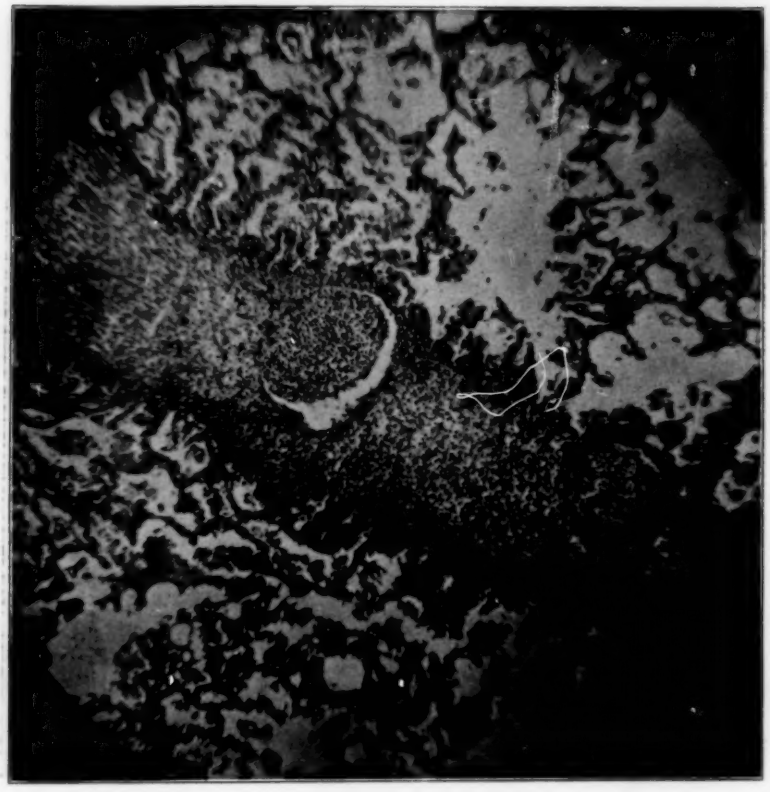


Fig. 4.—Section of lung from a case of interstitial pneumonia caused by the hemolytic streptococcus.

The question might here be raised whether it is not desirable to drop the term pneumonia as used to cover a pathologic condition so variable in its manifestations and etiology. Careful reading of reports from various hospitals leads to the firm belief that the clinical diagnosis in a large percentage of cases cannot be made to conform with the pathologic lesion — lobar pneumonia, bronchopneumonia and inter-

stitial pneumonia. Medical men, generally, have used the terms lobar and bronchopneumonia rather loosely, the diagnosis usually being based on the presence of consolidation of a part or the whole of one or more lobes.

In spite of the reports made by such workers as Cole and his associates at the Rockefeller Institute, knowledge of the bacteriology of pneumonia has been rather vague. With the unhappy experience with pneumonia, in both civil life and in the army, especially in the fall of 1918, large numbers of medical men have come in contact with the disease in a form exceeding in amount and variety of manifestations anything in their previous experience. If changes in the nomenclature can be made so as to indicate a difference in the prognosis, treatment and the complications to be looked for, much will be accomplished.

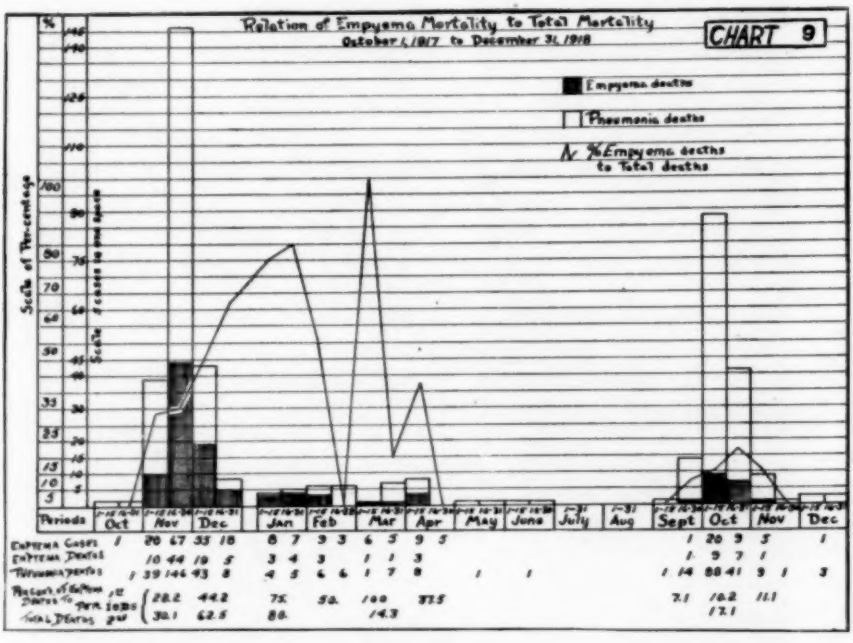
Another advantage would be attained in emphasizing the varieties of infecting organisms. The inclusion of pneumonia among the acute infectious diseases is comparatively recent. It is probable that the day of treating such cases in a general medical ward is past, and yet we have scarcely entered into the practice of isolating the various types of pneumonia. It is just as undesirable to expose a case of "acute lobar pneumonia," to an "acute streptococcus pneumonitis" as to expose any general medical case to either of the above. Isolation of the various types of pneumonia will probably be practiced generally in all well conducted hospitals. In such places with adequate laboratory facilities there will be no reason for doing otherwise.

In private practice it is probable that the average physician must look to the state or municipal laboratory for sputum type differentiation, as he now does for examination for Klebs-Loeffler bacilli. Unquestionably, some health departments will provide specific serum, and provide for its administration. Such type differentiations, when incorporated as a part of the diagnosis, will serve to accentuate the importance of avoiding cross infections by using all the present methods of prophylaxis and stimulating their further development. Would it not, therefore, be well to do as has been done with "rheumatism"— reserve the diagnosis "acute lobar pneumonia" for those cases of epidemic pneumonia which are fairly well defined clinically, and due either to Type I pneumococcus, with its specific serum, or to the fixed types of pneumococci, I, II and III, and apply the term "acute pneumonitis," giving the causative organism whenever possible, to the various other conditions now called lobar, interstitial, lobular pneumonia or bronchopneumonia, septic or terminal pneumonia, etc.?[2]

2. Hamburger and Fox in reporting on pneumococcus and streptococcus infections at Camp Zachary Taylor used the term "pneumonitis."

COMPLICATIONS

Empyema: Of the 2,344 cases of pneumonia, 249 developed empyema, an incidence of 10.6 per cent. This incidence was a steadily decreasing one for the three periods, being 16.5, 9.5 and 4.3 per cent., respectively. Period 1 furnished 41.5 per cent. of the total pneumonias, and 64.6 per cent. of the total cases of empyema, whereas Period 3 furnished 35.5 per cent. of the total pneumonias, and only 14.4 per cent. of the total empyemas.



DIAGNOSIS

The diagnosis of pus in the chest is very difficult in certain cases, much less so in others. This depends largely on the character, amount and location of the effusion, and whether or not it occurs early or late in the course of the pneumonia. Its recognition often demands all the aids to diagnosis that can be summoned. The diagnosis rests on one or more of the following: (*a*) Change in condition of patient; (*b*) physical signs; (*c*) roentgenography and fluoroscopy; (*d*) sometimes, though not often, a change in the leukocyte count and increase in the number of polynuclear cells may be helpful.

(*a*) Change in Condition of Patient: During the course of the pneumonia there comes a time, usually between five and ten days, when in the absence of extension of the process the temperature, together with the pulse and respiratory rates, should fall, either by crisis or lysis. If this fails to occur, and especially if the remissions increase, suspicion should be aroused. In some cases the temperature falls to normal; after a varying number of days an afternoon rise of temperature begins. We have had cases in which pus was present where the temperature fell to normal after the primary pneumonia, and did not rise again above 99 F. until after the pus had been evacuated. Chills and sweating have been rare. Where the rise in temperature persists, or when convalescence is slow, pus must always be suspected. Many cases have ultimately been diagnosed where the first suspicion was raised by the very slow convalescence and the presence of pus or tuberculosis were considered most probable.

(*b*) Physical Signs: The physical signs have been notably irregular, and no wonder when one considers the multiplicity of conditions existing. The fluid may vary from a thin, dirty (dishwater) serofibrinous exudate, slightly greenish in color, as in the early hemolytic streptococcus fluids, to a dense creamy pus in some pneumococcic infections. In between are all gradations.

In our experience dulness, with a change in breath and voice sounds, sometimes a diminution, more frequently bronchophony or egophony, are the best indications for requesting a roentgen-ray examination, even though this may be limited to a fluoroscopy.

With supporting evidence from these aids, and sometimes without, no hesitation has been felt in inserting a needle one or many times. In many hundred cases needled, the only mishap has been the occasional entrance of air into the pleural cavity, which was of no serious import. A particular precaution we have practiced is that the needle, once inserted, is always withdrawn to the inner surface of the chest wall before changing the direction in order to explore a different area. This is done to avoid tearing the lung tissue. The point of insertion is over the area of maximum signs, since the rule rather than the exception is for the pus to be pocketed. In a few cases marked sensitiveness on percussion has helped to locate the pus.

Often signs are misleading, but a good rule is to insert the needle if there is a reasonable basis for believing pus to be present. Fluid has been obtained in areas over which there was dulness rather than flatness, with a friction rub and vocal fremitus present, and little change in voice or breath sounds. On the other hand, areas over which there was flatness, absence of vocal fremitus and markedly

diminished breath sounds, have frequently failed to show fluid. In the latter case the probability is that there was a dense fibrinous pleurisy, with little serous element. Sometimes, after a dry tap, a small drop of pus has appeared at the site of the puncture following the withdrawal of the needle.

(*c*) Roentgen-Ray Examination: The use of the roentgen ray has been of the greatest assistance in diagnosis.

The relation of the organism found in the pleural fluid to the predominant organism of the sputum is shown in Table 14. The mortality of 19 per cent. in pneumococcus infections, as compared with 33 per cent. in streptococcus and mixed infections, is in accord with the situation as reported from many other hospitals.

Table 15 gives the procedure in empyema for all periods. Of the 221 cases diagnosed previous to death, 150, or 67.9 per cent., occurred in Period 1. Of these 150 patients, 121 were operated on, with a mortality of 34 per cent. Of the twenty-nine patients not operated on, twenty-six died, a mortality of 89 per cent. Twenty-one of the twenty-nine died after the diagnostic puncture. These men were practically moribund at the time of diagnosis, too sick to withstand the shock of operation. The operation of choice has varied with the several chiefs of the surgical section. In Period I it was costatectomy, thoracotomy being done in the bad risks. Of the fifteen patients on whom a thoracotomy was done, eleven died, a mortality of 73 per cent.

Choice of the Time of Operation: As in most hospitals, the early practice was to operate as soon as the diagnosis was established. The result was a very high immediate operative mortality. In the streptococcus infections, especially where a purulent pleuritis developed early, prompt operation usually meant a collapsed lung on the operated side, and very possibly the opposite lung was consolidated, with little functioning lung tissue remaining. These operations, performed at the height of the toxemia, meant death, either from shock or asphyxiation. With this experience in view, aspiration was done every second day for a certain period and the intervals gradually increased thereafter.

The transition from the thin fluids commonly present in the streptococcus infections to a thick pus, occurs in a variable time. Frequently this has occurred in forty-eight hours. Ten to twelve days is the most frequent interval. Generally speaking, the longer away it is possible to get from the acute infection, the more favorable the end result. If, by repeated aspirations, the general condition improves, these should be continued. In the average case the pus will ultimately become so thick as to render further aspiration impossible. In a certain number of cases, even though aspiration is still possible, the general condition of the patient becomes worse, the pulse rate increases, the temperature

becomes irregular, with an increasing height in the evening. Chills and sweating are rare in these cases.

In many cases, even with the general condition of the patient fairly satisfactory, the time will come when operation, with irrigation, promises a more rapid recovery than continuous aspiration. In Period 1 many patients were admitted with thick pus already formed, too thick to be withdrawn through a large needle. These patients were too sick to justify being sent to the roentgen-ray department for a picture.

Medical Care.—Postoperative care, aside from careful attention to drainage and irrigation, is largely a medical one. Attention to nutrition, the question of cardiac stimulation, frequent and careful examinations of the chest for signs of accumulation of pus, pericardial effusions, etc., are the most important points. Later it is a matter of "conditioning," breathing and carefully graduated setting up exercises, hikes, games, etc.

In our opinion, this attention can best be given by retaining these patients on the Medical Section with one or more qualified surgeons assigned to this section for the necessary operative work, irrigations and dressings. It is essential that a man filled with enthusiasm for his work, and possessed of the necessary surgical technic, should receive such an assignment.

Metastatic Abscesses. — Metastatic abscess, single or multiple, occurred in seventeen cases of pneumonia. Of these seventeen cases four accompanied empyema. Five came to necropsy, three not being diagnosed before death. One of these undiagnosed cases was a small abscess in the first intercostal muscle; a second case was a perirenal abscess. The most interesting cases of this group were five cases in which a painless tumor was noted just above the symphysis pubis, not red and not tender to pressure. The first of these cases (Reg. No. 2422) was not recognized until there appeared a rounded tumefaction exactly in the midline, extending about two inches above the symphysis pubis. The tumor was thought to be a distended bladder, but on catheterization a very small amount of urine was obtained. One hundred cubic centimeters of salt solution was introduced into the bladder, and the same amount was withdrawn. The tumor was still present. The possibility of a diverticulum of the bladder was considered. There was no increase in temperature, and no muscular rigidity. During the next six days there was a slight, but constant, increase in the size of the tumor, the patient meanwhile voiding a normal amount of urine. On the sixth day fluctuation was obtained. An incision was made and about 150 c.c. of thick pus was found between the right rectus muscle and

its posterior sheath. Culture showed a pneumococcus—type undetermined. The other cases presented practically the same picture, except that in three the tumor was slightly asymmetrical.

Subcutaneous Emphysema.—Generalized subcutaneous emphysema, as a complication of pneumonia, occurred in eight cases, seven white men and one colored man. Three of these patients recovered.

The onset of the emphysema appeared to be definitely associated with an unusually severe paroxysm of coughing in one case. Hoarseness and increased dyspnea were the only symptoms apparently referable to this complication.

The tissues of the neck, posteriorly especially, but also in the supraclavicular region, were involved in all the eight cases; the interscapular region was involved in four; the axillae and pectoral region in three; the face in three; the flanks and thighs in one.

The three patients who recovered had a prolonged convalescence. Each one had a persistent hoarseness. Laryngeal examination showed only an acute laryngitis, which disappeared slowly. One patient has since been found to have pulmonary tuberculosis.

Anaerobic antemortem blood cultures were sterile in two cases; in the third case they showed pneumococcus—type undetermined.

Of the postmortem cases all showed emphysema of the mediastinal connective tissue, in addition to the evident subcutaneous emphysema noted during life. Petechial subpleural hemorrhages were evident in two cases. Free air beneath the visceral pleura, especially along the interlobular spaces and lung fissures, was seen in two cases. One case showed confluent patches of consolidation having undergone softening and produced abscess cavities. Microscopically, small areas of hemorrhage were frequent in these cases as in other pneumonia cases of the same period.

In addition there were ten cases of emphysema of mediastinal tissue diagnosed only at necropsy.

Bacteriologic study of the mediastinal tissue showing marked emphysema was attempted in eight cases with the following results on culture:

No growth	3
Pneumococcus Group IV	3
Streptococcus, nonhemolytic	1
Streptococcus, hemolytic	1

In each case the organism present was also found in the blood stream.

In one case with most marked subcutaneous emphysema before death, an emulsion of emphysematous tissue was injected intravenously

into a rabbit. The rabbit was killed in five minutes and placed in the incubator for eighteen hours. All organs, as well as heart's blood, gave a pneumococcus Group IV which was also isolated from the heart's blood of the patient.

SUMMARY

A large percentage of the cases of pneumonia here presented followed an epidemic of measles and an epidemic of influenza. Following the epidemic of measles, the predominance of hemolytic streptococcus as the infecting organism determined the high mortality and the high incidence of complications, especially empyema.

Following the epidemic of influenza the incidence of hemolytic streptococcus was less, but when present the lesions produced did not vary from those present in cases of the year previous. In addition to the streptococcus infections there was a large group of cases of mixed bacteriology with pneumococcus, especially Group IV, predominating.

During the greater part of the period, January to September, 1918, the character of the infection, mortality and complications were not essentially different from those occurring ordinarily. Throughout the first part of this period, pneumococci of fixed Types I and II were found in approximately the same proportion of cases as when these types were first described. From that time on they declined steadily until less than five per cent. of the cases showed their presence.

Definite evidence of the presence of the *B. influenzae* as a determining factor in pneumonias following the epidemic of the fall of 1918 was not obtained at this hospital. The epidemic, whatever its etiology, caused a lowering of resistance which favored invasion by organisms identical with those which observation during nonepidemic periods had shown to be present in the upper respiratory tract of individuals not suffering from pneumonia.

Postmortem studies show that the pneumococcus is constantly present in lobar pneumonia, while the hemolytic streptococcus, with a variety of other organisms, and the pneumococcus, is found in bronchopneumonia.

Comparison of sputum examinations with more accurate bacteriologic data from the same cases, has shown correspondence in a large percentage. If the sputum examination is made with a view to determining the predominating organism present, its value is greatly enhanced and in this form it is one of the valuable diagnostic procedures in pneumonia.

Clinical differentiation between lobar and bronchopneumonia to accord with postmortem findings has been impossible. For this reason it is suggested that the term acute pneumonitis, followed by a statement of the predominating organism in the sputum, be used to desig-

nate those cases of pneumonia which are not frankly lobar in type, but caused by one of the fixed types of pneumococcus.

The incidence of empyema was highest among the pneumonias following measles. For the entire period, cases complicated with empyema constituted 10.6 per cent. of the total pneumonias, and furnished 25.6 per cent. of the total pneumonia deaths.

The appearance of the pleural exudate caused by the *Streptococcus hemolyticus* was characteristic. Repeated aspiration of such fluids, followed by operation after the acute pneumonitis has subsided, has given the more satisfactory results at this hospital.

The occurrence of encapsulated pus was very common, especially in the streptococcus infections. These pockets were frequently multiple and offered great difficulties from an operative standpoint.

CRITERIONS FOR DISTINGUISHING THE ENDAMOEBA OF AMEBIASIS FROM OTHER ORGANISMS*

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The practitioner and clinical microscopist undertaking to make a critical diagnosis of the pathogenic ameba, *Endamoeba dysenteriae*, in either acute, chronic or latent amebiasis, is beset by certain practical and technical difficulties, which, under certain conditions, may become perplexing or even baffling, unless he has had some experience in dealing with the various forms of this ameba and its associated organisms of the human digestive tract. These difficulties have been cleared up somewhat, although the complexities of the situation have been increased somewhat, by the distinction of another very common, tetragenous ameba in human feces in addition to *E. dysenteriae*, by Wenyon and O'Conner,[1] namely, *Endamoeba nana*, a seemingly non-pathogenic species whose dimensions, number of nuclei, and clear pseudopodia do not differentiate it from the pathogenic form with which it may be associated. We have elsewhere shown[2] that this new endameba is the commonest intestinal ameba in American troops, in which we found 325 cases among 1,200 overseas troops, and ninety-two cases in 300 home service troops, a total of 417 in 1,500 men, or 28 per cent., while there were only 389, or 23 per cent., infections with *E. coli*, and 139, or 9.3 per cent., with *E. dysenteriae*. Of the latter, 130, or 10.8 per cent., occurred among the 1,200 overseas men.

From recent European findings and our own results it appears that *E. nana* in man has a very wide geographic distribution. In actual numbers its cysts far exceed those of the cysts of *E. coli* and *E. dysenteriae* in our experience. It is, therefore, to be expected that this endameba will appear rather frequently in stools examined in this

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* From the U. S. Army Laboratory, Port of Embarkation, New York City; Major E. H. Schorer, M. C., U. S. Army, officer-in-charge.

1. Wenyon, C. M., and O'Conner, F. W.: Spread and Incidence of Protozoal Infection in British Troops, J. Roy. Army Med. Corps, Lond. **28**:1, 1917.

2. Kofoid, C. A., Kornhauser, S. I. ,and Plate, J. F.: On Intestinal Parasites in Overseas and Home Service Troops of the U. S. Army, with Special Reference to Carriers of Amebiasis, J. A. M. A. **72**: 1919.

country, and the examiner must be prepared to distinguish *E. dysenteriae* not only from the well known *E. coli,* but also from this *E. nana.* The criterions employed in the former case are not applicable in the latter.

Moreover, there are several organisms whose cysts may have about the same size, from 7 to 10 microns in diameter, and are sometimes of the same spheroidal shape, at least in some of the individuals, and unstained or in iodin-eosin have much the same optical properties and colors, as the smaller races of *E. dysenteriae.* These organisms are the occasionally spheroidal cysts (Fig. 15) of *E. nana* (usually ellipsoidal), and those of the flagellate *Chilomastix mesnili* (Fig. 32) (usually pyriform), the larger and more rotund individuals of a large race or species (Fig. 35) of the common intestinal yeast (usually ellipsoidal), the central, homogeneous body of *Blastocystis hominis* (Fig. 33) in unstained material, and certain spheroidal spores of a mold (Fig. 43) occurring in stale stools. The ovoidal cysts of an unknown organism (Fig. 34), certain homogeneous spheres (Fig. 39), and leukocytes in various phases of degeneration, add to the complex of organisms or parts thereof, from which the cysts of the organism of amebiasis must be distinguished critically. Not infrequently *E. dysenteriae* occurs coincidently with one or both of the other two species. It was found with both in forty-one cases of the 130 infections found in 1,200 overseas troops, with *E. nana* only in forty-four cases, and with *E. coli* alone in fifteen cases. It was found without other endamebae in only thirty of the 130 cases of infection. Mixed infections with *E. dysenteriae* appear to be the rule rather than the exception.

FREE STAGES

In cases of acute amebic dysentery the large, free *E. dysenteriae* are readily distinguished from *E. coli* by their ingested red blood corpuscles, their clear, hyaline pseudopodia, and their very active locomotion. *E. coli* rarely ingests corpuscles, has granular pseudopodia, and is sluggish in movement. The smaller races of *E. dysenteriae* in the free state are to be distinguished from *E. nana* of comparable size in the free state with difficulty and mainly by the structure of the nucleus, preferably in stained preparations.

In a case of infection by *E. nana* alone which was under daily observation we have found that the free phase of the species appears rarely in the usual formed stools, but may occur in large numbers in liquid stools after a saline purge. In the sluggish free stage of formed stools the pseudopodia (Fig. 15) are single, broad, terminal on the elongated body, and hyaline. In the more liquid stools the amebas on the warm stage are very active and send out smaller, more slender,

hyaline pseudopodia in various directions. These pseudopodia seem to be more numerous and smaller than in *E. dysenteriae* of comparable size but are not always so and do not afford a critical criterion for distinguishing them from *E. dysenteriae,* owing to their variability with the physiologic state of the individual ameba. The presence of highly refractive, bacteria-filled food vacuoles in *E. nana* is sometimes of value as indicating the probability that the ameba in question is that species, but these vacuoles are quite variable in appearance and occurrence and are therefore somewhat unreliable as a criterion.

There is always available, however, an absolutely diagnostic criterion for the separation of the free stages of *E. dysenteriae* from those of *E. nana,* namely, the structure of the nucleus as it appears in the stained slide. In *E. dysenteriae* (Figs. 1-11) there is a central karyosome and the peripheral chromatin is scattered over the nuclear membrane somewhat uniformly in plaques or granules of small size. In *E. nana* (Figs. 12-23) there is no central granule and the peripheral chromatin is massed in a single large clump at one point on the nuclear membrane. These nuclear contrasts may sometimes be made out in the living material or in iodin-eosin, but are perfectly distinct in amebas stained in iron hematoxylin.

ENCYSTED STAGES

In cases of chronic and latent intestinal amebiasis, and in carriers, the evidence of infection will be determined mainly by the encysted stages which occur in formed stools, or in the semifluid ones which often characterize such cases. Free amebas are usually rare or absent in such stools. The determination of infection in such cases rests wholly on the microscopic analysis of the encysted stages of these intestinal amebas and associated organisms of the digestive tract.

Methods.—The most useful method for this analysis, in our experience, has been the direct smear with Donaldson's[3] iodin-eosin stain. The original formula for this is as follows: Five per cent. aqueous solution of potassium iodid saturated with iodin, one part; saturated aqueous solution of either eosin or Rubin S, one part. Mixed fresh each morning.

By a curious error reviews of this paper in the *Tropical Disease Bulletin* and the *Bulletin of the Institute Pasteur* add ether to this formula. We have found in practice that the volumes of the component solutions may be modified to advantage, owing, perhaps, to varying efficiency of the eosin. We have made these solutions in physiologic salt solution and reduced the proportion of iodin as fol-

3. Donaldson, R.: Method of Detecting Protozoal Cysts in Feces by Means of Wet Stained Preparations, Lancet **2**:571, 1917.

lows: Saturated solution eosin in normal salt solution, two parts; 5 per cent. potassium iodid in normal salt solution saturated with iodin, one part; normal salt solution, two parts.

The smear is prepared for microscopic examination by rubbing out a minute bit of the feces by rolling it on a round applicator stick in a small drop of normal salt solution and then in an adjacent drop of iodin-eosin stain. A single cover is placed on both drops and the smear is ready for immediate examination. Living flagellates and unstained cysts appear in the unstained part. In the stained area the bacteria, fecal particles and the intestinal yeasts (except the larger forms) stain at once. Against the pink background the protozoan cysts stand out clearly as bright spherules which soon become tinged with the iodin to varying tones of yellow, while their glycogen filled vacuoles, when present, turn light or dark brown according to their mass. The nuclei become more clearly defined as the iodin penetrates, especially in *E. coli* and *E. dysenteriae*. They are detected with difficulty in this stain in *E. nana*.

We have used the concentration method of Cropper and Rowe[4] as modified by Boeck[5] on over 1,500 stools, as supplemental to the direct smear, but have added less than 10 per cent. to the infections detected by the direct smears. A few trials of the Carles-Barthelmy[6] citric formalin method have also been made. These added infections have been mainly of *E. coli*, which is rarely abundant, a few light infections of *E. nana* and a few cases of *Giardia*. It is probable that the detection of light infections of *E. dysenteriae* would be facilitated by these methods, but the time required is greater and the percentage of infection of pathogenic organisms detected thereby very small. The direct smear is simple, rapid and in our experience both efficient and reliable for practical purposes. Concentration methods are useful in research and in following up difficult and suspected cases.

CRITERIONS FOR DISTINGUSHING INTESTINAL ENDAMEBAS

The following tabular view of the distinctions will facilitate quick comparison of the diagnostic features of the species of endameba. The analyses made by Dobell and Jepps,[7] Mathews[8] and Smith[9] have

4. Cropper, J. W., and Rowe, R. W. H.: A Method of Concentrating Entameba Cysts in Stools, Lancet **2**:63, 1917.

5. Boeck, W. C.: Rapid Method for Detection of Protozoan Cysts in Mammalian Feces, Univ. Calif. Pub. Zool. **18**:145, 1917.

6. Carles, J., and Barthelmy, E.: Procéde special pour collecter les kystes dysenteriques contenus dans les selles, C. R. Soc. Biol., Paris, **80**:402, 1917.

7. Dobell, C., and Jepps, M. W.: On the Common Intestinal Entamebas of Man, and Their Differential Diagnosis, Brit. M. J. **1**:607, 1917.

8. Mathews, J. K.: Observations on the Cysts of the Common Intestinal Protozoa of Man, Ann. Trop. M. & Parasitol. **12**:17, 1918.

9. Smith, A. M.: Measurements and Observations on the Cysts of *Entameba histolytica* and *Entameba coli*, Ann. Trop. M. & Parasitol. **12**:27, 1918.

been helpful in its preparation. In this table the criterions are stated succinctly without the essential qualifications which will be discussed later.

TABLE 1.—DIAGNOSTIC FEATURES OF ENDAMOEBA DYSENTERIAE, E. NANA AND E. COLI

Criterion	E. dysenteriae	E. nana	E. coli
Size	(5) 6-15 (20) microns	(3) 5-12 (16) microns	(11) 14-22 (35) microns
Shape	Spheroidal, sometimes asymmetrically rounded	Ellipsoidal in smaller forms, ovoidal in larger; frequently irregular, sometimes spherical	Spheroidal, sometimes ellipsoidal, ovoidal or irregular
Optical properties, unstained	Most highly refractive, glassy, often irregularly vacuolated; light grayish blue; nuclei rarely visible; glycogen mass not visible.	Less highly refractive but with highly refractive granules, grayish blue; nuclei invisible; glycogen mass distinct	Least highly refractive, homogeneous, porcellanous, grayish blue; nuclei faintly visible; glycogen mass faintly visible
Stained with iodin-eosin	Cytoplasm bright greenish yellow; coarsely vacuolated, in small races evenly but finely granular	Cytoplasm greenish yellow with numerous small refractive vacuoles	Cytoplasm coarsely uniformly granular; yellowish brown
	Nuclei distinct with highly refractive, thick border and distinct central granule	Nuclei indistinct, with thin border and peripheral chromatin blob	Nuclei very distinct with thin granular borders and central granule
	Glycogen diffuse; if massed, with vague limits	Glycogen dense, in one or more large sharply defined masses, seldom central	Glycogen central with vague borders
	Cyst stains red more quickly	Cyst resists stain longer	Cyst usually resists stain longer
Nuclei: number	1—30-45% 2—13-30% 3—rare 4—25-55%	1—Very common 2—Less common 4—Common in small race, very rare in large one	1—Very rare 2—Rare 4—Very rare 8—Very common 16—Very rare
Structure	Central granule distinct; peripheral chromatin distributed rather evenly in small plaques	No central granule; nuclear membrane indistinct; peripheral chromatin gathered in a single blob on the membrane	Central granule distinct, peripheral chromatin in a few large plaques on the nuclear membrane
Chromatoid substance	In one stout bar or several slender bars with rounded ends. Present in about 50% of the cysts	In several rounded or irregular masses. Rarely present	In stout or slender splinters with square or sharp ends. Present in about 5-10% of the cysts
Cyst wall	Thin, distinct	Variable, less distinct	Thicker, very distinct
Size races	Very evident. Small race at 7 microns, large race at 13-14 microns, and one at 10 microns are the most frequent	Very evident. One at 5-7 microns, and one at 8-10 microns, and probably a still larger one at 12-15 microns, most frequent	Less evident. Probably one at 15, one at 18 microns and one larger

The table shows far less fully than the material itself the great variability in the criterions which are available to distinguish these three species. It should be borne in mind, however, that every case of infection will generally afford some individual amebas on which

a diagnosis may be made clearly and unequivocally, although there may be some individuals that are indeterminate and others of questionable allocation. Abnormal, moribund and pathologic states are to be expected in these parasitic species.

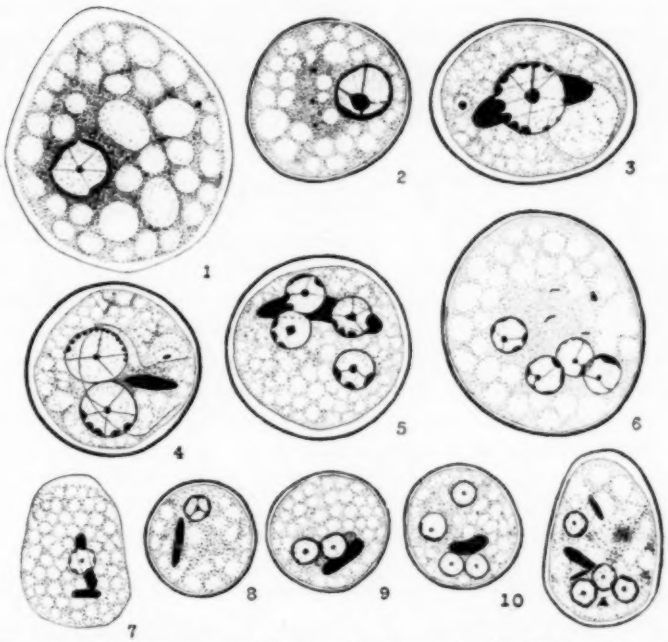
Infections of *E. coli* are usually readily distinguished at once in iodin-eosin by size, color and granulations of the cytoplasm, as well as by the prevalent eight nucleate cysts. Individuals are relatively rare in most infections by this ameba.

Infections by *E. nana* are distinguished by the abundance of cysts, the large, clearly defined glycogen mass when present, the prevalence of ellipsoidal or ovoidal cysts, the abundance of highly refractive granules, and, preferably in stained material, the absence of central granule and the clumping of the chromatin on the nuclear membrane in a single blob.

In infections by *E. dysenteriae* the cysts are generally less abundant than in those by *E. nana,* and are distinguished by their glassy, refractive, irregularly vacuolated or (in small cysts) almost homogeneous cytoplasm, with distinct nuclei with central granule and heavy rim, never exceeding four in number, with relatively abundant mononucleates and glycogen, when present, diffusely distributed.

ENDAMOEBA DYSENTERIAE

Cysts are usually spherical and fall into three general groups according to size, the largest being from 12 to 14 microns in diameter and the smallest from 7 to 8 microns. A medium sized race of from 10 to 11 microns is less abundant. However, individuals ranging from 5 to 20 microns may be found. The cyst wall is thin and rather easily penetrated by the iodin-eosin stain and by hematoxylin stains. In the iodin-eosin stain the cytoplasm is first a bluish gray which changes to a yellow and then to a pink color, which gradually deepens to red. The cytoplasm is unevenly vacuolated and is very finely granular but the granules are not so evenly distributed as in *E. coli.* The glycogen mass, when present, stains a light brown in iodin-eosin, the edges gradually shading into the surrounding cytoplasm. Sometimes its glycogen is diffused throughout the entire cyst which then stains a yellowish brown color. Chromatoid rods are found in a majority of the cysts, represented by either one large rod with blunt ends nearly the diameter of the cyst in length, or by several smaller rods scattered irregularly in the cytoplasm. These rods are seen in a 0.01 per cent. solution of Janus green in physiologic salt solution after a few minutes application as definite, bluish, highly refractive bodies with clear cut outline. They also stain deep black in Heidenhain's iron hematoxylin.



Figs. 1 to 6.*—Large races of *Endamoeba dysenteriae* (10-17 microns) stained with iron hematoxylin, ×2800. (1) Relatively small, free ameba in contracted condition, showing clear, peripheral ectoplasm; 17 microns. (2) Mononucleate cyst with peripheral chromatin uncontracted and no chromatoidal body; 10 microns. (3) Same, with large, stout chromatoidal rod; chromatin on nuclear membrane gathered in small clumps; large glycogen vacuole in cytoplasm; 10 by 13 microns; (4) Binucleate cyst with small, fusiform chromatoidal rod and slender, coiled thread; 11 microns. (5) Quadrinucleate or tetragenous cyst with large chromatoidal rod; 12 microns. (6) Largest race of *E. dysenteriae* four nuclei; no chromatoidal rod; 14 microns.

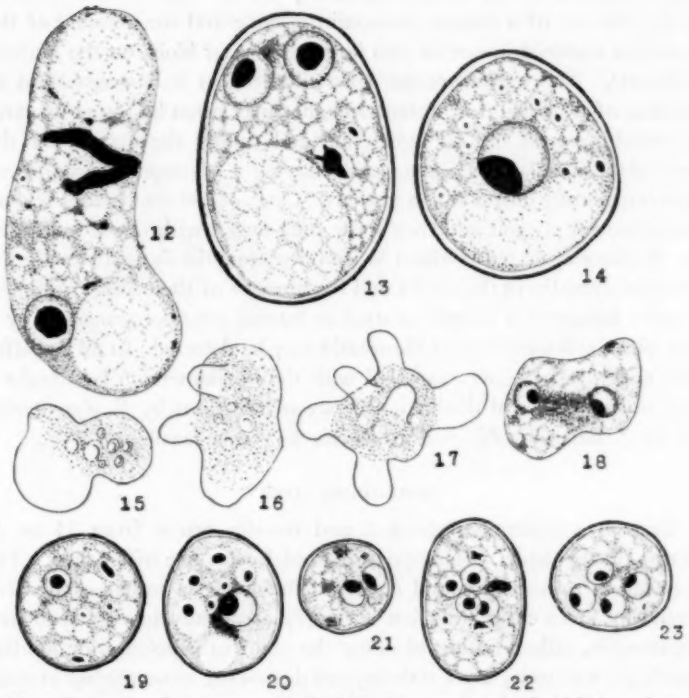
Figs. 7 to 11.—Small races of *Endamoeba dysenteriae* (7-10 microns) stained with iron hematoxylin, ×2800. (7) Small, free ameba evidently approaching encystment; two chromatoidal bodies; 7 by 10 microns. (8) Small mononucleate cyst with slender chromatoidal bar; 7 microns. (9) Small binucleate cyst with two chromatoidal bars; 8 microns. (10) Small quadrinucleate cyst with stout chromatoidal body; 8 microns. (11) Ovoidal cyst with four nuclei and three chromatoidal bars; 7 by 11 microns.

*All drawings have been made by Dr. Olive Swezy under a grant from the Division of Medicine and Related Sciences, National Council of Research.

The nuclei are one to four in number. They should appear distinct and well defined in cysts penetrated by iodin-eosin stain. The chromatin appears to be evenly distributed on the nuclear membrane which seems to be thicker than in *E. coli,* and there is present a distinct central granule. At sharp focus each nucleus should be seen as an even circle of highly refractive material, with a clearly defined central dot. A critical examination of the nuclei is absolutely essential in making the determination. It is advisable to roll the cyst by a slight pressure on the cover glass, so that the nuclei may be studied from various angles, counted and proved to be characteristic for *E. dysenteriae.* Cysts of small races are at times difficult to determine and permanent hematoxylin preparations may be necessary to arrive at a definite conclusion. In iron hematoxylin preparations the nuclei stain very definitely after fixation in modified Schaudinn's fluid. The peripheral chromatin does not appear so evenly distributed on the nuclear membrane as in cysts stained by iodin-eosin, being found as many more or less irregularly rounded plaques having small spaces between. This may be due in part to the method of fixation. The central granule is very definite and from it fibrils radiate to the chromatin plaques on the nuclear membrane. The fibrils often show a single granulelike thickening some distance from their central attachment. Unlike *E. coli* the nuclear material of this species takes a deep black stain readily.

ENDAMOEBA NANA

Cysts are generally ovoidal or ellipsoidal but are occasionally spheroidal. The larger races are from 10 to 15 microns in diameter and usually ovoidal, the smaller races are from 4 to 8 microns and ellipsoidal. The cyst wall is thin but distinct and is not easily penetrated by iodin-eosin stain, the cytoplasm remaining for a time grayish green. Glycogen is most abundant in large mononucleates and when present stains deep brown, showing that the iodin of the stain has penetrated but the eosin is excluded for many minutes. Dead cysts, however, stain deep red very quickly. *Endamoeba nana* stains well with iron hematoxylin. The cytoplasm contains many small vacuoles enclosing bacteria. These vacuoles are highly refractive and obscure the nuclei. The glycogen mass, which is frequently present, has a very definite outline, not shading into the surrounding cytoplasm, and is lateral in position. This mass dissolves out in the iron hematoxylin preparations, leaving a clear vacuole. The chromatoid body is made up of a mass of small rods irregularly clumped together, or in an amorphous mass. These may be seen in the hematoxylin preparations and some individuals are crowded with small chromatoidal granules.



Figs. 12 to 14.—Large race of *Endamoeba nana*, stained with iron hematoxylin, × 2800. (12) Sluggish, free ameba from formed stool, mononucleate with two empty glycogen vacuoles, a large, irregular chromatoidal rod, and several bacteria-filled food vacuoles. Chromatin clump of nucleus in face view; 9 by 22 microns. (13) Large, mononucleate cyst with glycogen vacuole, numerous food vacuoles, and chromatin clump in side view; 12 by 13 microns. (14) Binucleate cyst with large glycogen vacuole, large food vacuole, and chromatin clump in face view; 11 by 17 microns.

Figs. 15 to 23.—Small race of *Endamoeba nana* (6-8 microns), stained with iron hematoxylin, except figures 15 to 17, which were drawn from living specimens; × 2800 (15, 16, 17). Three successive positions of a small *E. nana*, from stool after saline purge, on warm stage; 8 to 10 microns. (18) Sluggish, binucleate, free ameba with oblique and lateral views of peripheral chromatin clump; 5 by 9 microns. (19) Mononucleate cyst with several food vacuoles and no glycogen vacuole of chromatoidal body; 7 microns. (20) The same with small glycogen vacuole, numerous food vacuoles and no chromatoidal rod; 7 by 8.5 microns. (21) Minute binucleate cyst; 5.5 microns. (22) Ellipsoidal cyst with four nuclei; chromatin clumps in face view, three food vacuoles and an irregular chromatoidal body, 7 by 9 microns. (23) Quadrinucleate cyst with chromatin clumps in side or oblique view; 7 microns.

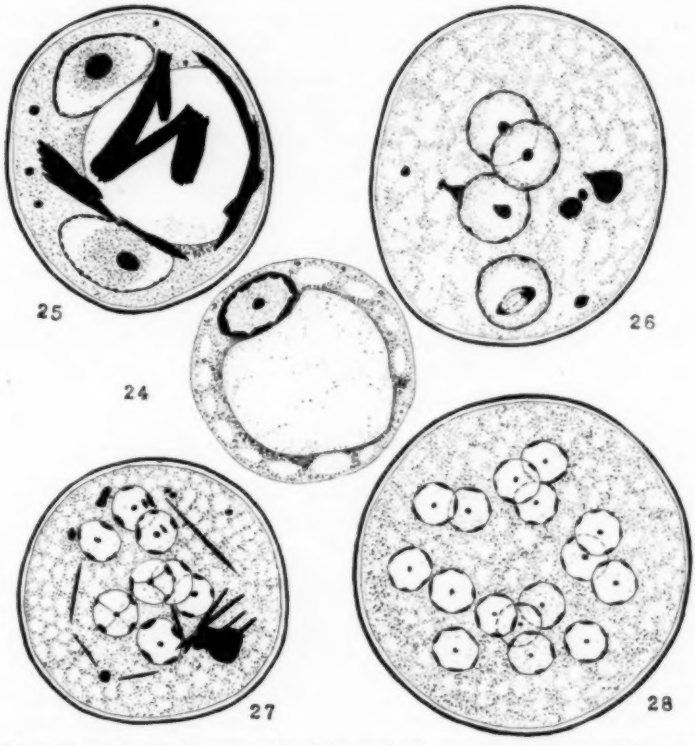
The nuclei are one to four in number and their structure forms the most important means of distinguishing the species. The characters are the absence of a central chromatin granule and the massing of the chromatin material in one or two large clumps or blobs on the nuclear membrane. The nuclei are not so easily seen in iodin-eosin stain as are those of *E. coli* and *E. dysenteriae,* but may often be found by careful searching with the oil immersion and rolling the cyst under the cover glass. In large *E. nana* cysts having a glycogen mass present there is generally only a single nucleus. Cysts of the small races seldom have glycogen present and they show four nuclei with massed chromatin. *E. nana* cysts well stained in iron hematoxylin show distinctly the massed chromatin in the nuclei and the absence of the central granules. In some instances a minute central or lateral granule connected by a fiber with the lateral blob of chromatin may be detected. In all doubtful cases such preparations examined with the oil immersion lens make a clear and unequivocal distinction between infections by *E. dysenteriae* and by *E. nana* possible and a definite diagnosis feasible.

ENDAMOEBA COLI

Cysts are generally spherical and usually range from 14 to 22 microns in diameter. Elongated ellipsoidal cysts are often seen. The cyst wall is rather thick and clearly defined. It is rather easily penetrated by iodin-eosin stain but acts very erratically in regard to iron hematoxylin, either failing to allow the stain to penetrate, or holding it with great tenacity after staining and destaining more readily in some instances. In iodin-eosin stain the cyst first appears greenish yellow and may be picked up with the low power, standing out clearly against the pink background. Gradually, the color changes to a yellowish green and then to a light brown, but it is less readily tinged by the eosin of the stain than is *E. dysenteriae.* The cytoplasm is more coarsely but more uniformly granular than that of *E. dysenteriae.* The vacuolization in the eight-nucleate cysts is very uniform. Glycogen is rarely present except in cysts having fewer than eight nuclei. In binucleate cysts the glycogen appears in iodin-eosin stain as a large, squarish, rather definitely defined dark brown mass, filling the greater part of the cyst and crowding the two large, elongated nuclei peripherally in the cyst. The chromatoid bodies are rarely seen. In Janus green and in iron hematoxylin they appear, when present, as several sharp, pointed splinters lying in various directions in the cytoplasm of the cyst.

The nuclei are generally eight in number, but exceptionally large cysts may contain sixteen. They appear clear and definite in iodin-eosin stain and may be counted and studied without great difficulty.

Each nucleus has a central granule and peripheral chromatin situated in the nuclear membrane in uneven masses, giving, at sharp focus, a rather ragged inner edge to the refractive ring of chromatin material. In *E. dysenteriae* this inner edge is more even. In hematoxylin the nuclei are generally not so distinct as those of *E. dysenteriae* treated by

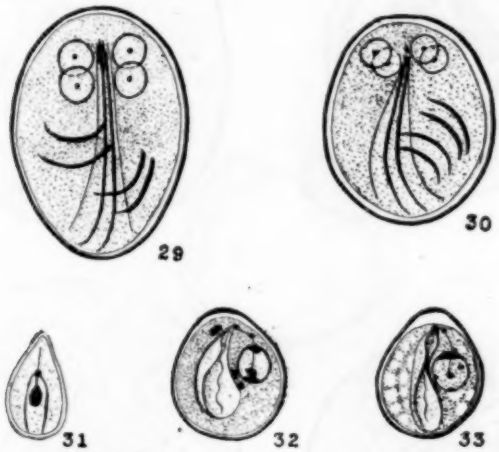


Figs. 24 to 28.—*Endamoeba coli*, stained with iron hematoxylin, × 2800. (24) Mononucleate cyst with large glycogen vacuole; 12.5 microns. (25) Binucleate cyst; 15 by 17 microns. (26) Quadrinucleate cyst with irregular, deeply stained masses in the cytoplasm. Nuclei apparently in mitosis; 18 by 20 microns. (27) Cyst with eight nuclei, chromatoidal splinters, and deeply stained masses; 15 microns. (28) Cyst with sixteen nuclei. No chromatoidal splinters; 19 microns.

the same method, as the cyst either decolorizes too much or retains the stain throughout. For this reason the picture given by iodin-eosin is more distinct and therefore more satisfactory than that given by iron hematoxylin, especially in slides decolorized for *E. dysenteriae*.

INTESTINAL FLAGELLATES: CHILOMASTIX MESNILI

The cysts of this flagellate (Figs. 29 and 30) are typically pyriform but are sometimes spherical, in which case they resemble superficially mononucleate *E. dysenteriae*. They often have diffuse or feebly massed glycogen, and sometimes show scattered, ellipsoidal chromatoidal inclusions in iron hematoxylin stain. The nucleus has a subcentral granule and massed peripheral chromatin. The most characteristic feature is the cytostomal or oral loop, which forms a characteristic dark, flattened ring visible in iodin-eosin stain in favorably oriented cysts. There



Figs. 29 to 33.—Flagellate cysts stained with iron hematoxylin, ×2800. (29) Large cyst of *Giardia intestinalis* with two zooids; four anterior nuclei, two axostyles and postero-lateral intra-cytoplasmic flagella, and two pairs of parabasal bodies; 14 microns. (30) Smaller, globose race of the same; 12 microns. (31) Cyst of *Waskia intestinalis*. (After Wenyon and O'Connor, 1917, pl. 4, fig. 15); 6 microns. (32) Ovoidal cyst of the same; 7.5 microns. (33) Pyriform cyst of *Chilomastix mesnili*, with cytostomal loop surrounding undulating membrane, anterior blepharoplast with rhizoplast running to nucleus and chromatin plaque; 7.5 microns.

appears to be only a single nucleus in the cysts. This is the most confusing cyst encountered in stools when spheroidal or ellipsoidal in shape, as it appears to be in some cases. It can usually be determined in heavily stained cysts in iodin-eosin stain under the oil immersion by rolling the cyst into favorable position for inspection. In pyriform cysts the wall is thickened slightly at the top. Its largest diameter is from 6 to 9 microns, thus establishing a ready basis for confusion with small ellipsoidal cysts of *E. dysenteriae* and *E. nana*. This is the most abundant flagellate cyst in human stools next to those of *Giardia*.

WASKIA INTESTINALIS

This flagellate (Fig. 31), described by Wenyon and O'Connor[1] from Egypt, occurs rarely in our records. Its free state appears in liquid stools and its cysts less frequently in formed stools. Its cysts are of the same type as those of *Chilomastix* but are more slender and tapering, with the internal structure less clearly defined.

GIARDIA INTESTINALIS

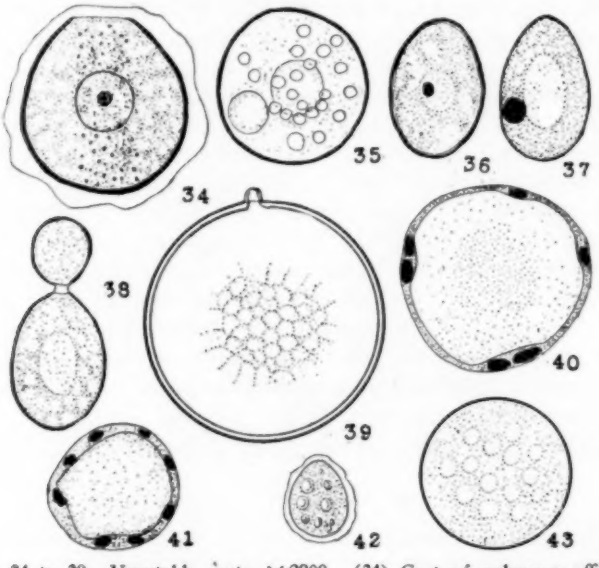
Cysts of this common flagellate (Figs. 29 and 30) occur often in great numbers and in cyclic recurrence in cases of infection. There are two races, one with a short ellipsoidal to subspheroidal cyst, about 10 to 12 microns in length, and a more common one with longer, more slender cysts, 12 to 14 microns in length. They can be distinguished very readily by their shape, their partially separated cyst wall, and especially by the two or four, usually polar, nuclei, the curved, longitudinal axostyles, and the one or two pairs of curved, comma-shaped parabasal bodies. They resist iodin-eosin stain for some time, but unevenly in different cysts, some staining dark brown rather quickly and others not at all. In destaining in iron hematoxylin these cysts usually lose most of their stain before the intestinal amebas are properly decolorized, and are often shrunken in appearance. It is not unusual to find many dead, abnormal and shrunken cysts in fresh stools which stain quickly with eosin.

Cysts of *Trichomonas intestinalis* are unknown.

VEGETABLE ORGANISMS: BLASTOCYSTIS HOMINIS

This organism (Figs. 40, 41 and 42), next to the intestinal yeasts, is the most abundant organism here discussed. It usually accompanies other protozoan infections. In examinations of 1,120 stools with 440 infections with this organism, it occurred alone in 116 instances or 27 per cent. only. In other cases it accompanied *Giardia, Chilomastix,* an intestinal ameba, or some combination of these organisms. It is exceedingly variable in size, from 3 to 20 microns, and in shape, as well as in its reactions to stains. While generally spheroidal in the larger sizes the small primary stages are often ellipsoidal, thus resembling *E. nana.* The larger stages have a central homogeneous mass, highly refractive and with the optical appearances of protozoan cysts, while the peripheral cytoplasm is very transparent and may be surrounded by an unstainable, extraordinarily hyaline, mucous coat. The spheroidal central mass sometimes takes on an angular contour. The outer, granular, protoplasmic sheath stains pink in iodin-eosin stain, which brings out the refractive granules of the sheath and thus reveals the true nature

of the organism. The central area takes up little eosin. The minute primary cysts have no such central mass but granular material fills this region which takes on a yellow color in iodin-eosin stain. Their granulations and their ellipsoidal or oval shape renders them extraordinarily similar to *E. nana*. The thin pink film, visible after exposure to iodin-eosin stain, which surrounds these primary cysts (Alexeieff[10]) reveals their probable relation to *Blastocystis hominis*. This organism appears in literature as the cyst of *Trichomonas*.



Figs. 34 to 39.—Vegetable cysts, ×2800. (34) Cyst of unknown affinities; iodin-eosin; 9 microns. (35) Large race of spheroidal yeast with central vacuole; iodin-eosin; 8 microns. (36) Common intestinal yeast with subcentral vacuole and lateral deeply stained granule below; iron hematoxylin; 7 microns. (37) Same with granule at the side; 7 microns. (38) Budding yeast; iodin-eosin; 7 microns. (39) Homogeneous cyst of unknown relations, yeast or phycomycete with trace of budding; iodin-eosin; 13 microns.

Figs. 40 to 42.—*Blastocystis hominis*. (40) Secondary stage with large central vacuole with homogeneous contents; 10 microns; iron hematoxylin. (41) Small stage of the same; 7 microns. (42) Minute primary stage with granular center and peripheral film; 5 microns; iodin-eosin.

Fig. 43.—Spheroidal phase of an intestinal mold; 8 microns; iodin-eosin.

There are certain large forms which are evenly and coarsely granular in the central region which then stains a dark red color with iodin-eosin stain. They appear to be forms of *Blastocystis*.

10. Alexeieff, A.: Sur les "Kystes de *Trichomonas intestinalis*" dans l'intestin des Batraciens, Bull. Sc., France et Belgique **44**:333, 1911.

HOMOGENEOUS CYSTS

In many stools there occur spheroidal cysts (Fig. 39) from 6 to 20, rarely 30 microns in diameter, which in unstained smears are sometimes brownish as though tinged by iodin or bile. They have a typical cyst wall and vary in content from a homogeneous, undifferentiated, substance resembling cytoplasm to numerous phases of vacuolation. Rarely a structure resembling a nucleus is found. It is possible that they represent degenerative phases of one or several organisms of the digestive tract or of cysts or spores habitually contaminating the food, instead of a distinct organism. The nature of their occurrence indicates a relationship to some normal inhabitant of the digestive tract. These problematical structures appear to be included in the "iodin cysts" of Wenyon and others as the "cysts without iodophylic body." The published figures of these "iodin cysts" suggest that these cysts with iodophilic body are a large race of *E. nana*. These homogeneous cysts are probably the chlamydospores of a phycomycete or resting stages of a yeast.

In iodin-eosin stain the color is intensified, but in our experience they do not contain localized glycogen or brown-staining vacuoles. Not infrequently there is a small protuberance at one point where the wall is thin, suggesting a yeast-like budding.

INTESTINAL YEASTS

The most abundant organism here considered is an intestinal yeast (Figs. 34 to 38) normal to the human digestive tract. It occurs in practically every stool, in varying degrees of abundance. It appears, as a rule, in the form of a small ellipsoidal organism with a slightly excentric light area and adjacent granule in the granular cytoplasm and a heavy wall. It stains red promptly in neutral red or in iodin-eosin, and is thus at once separated from protozoan cysts. The yeasts are floated off by concentration methods. They are exceedingly variable in their reaction to iron hematoxylin, usually decolorizing entirely or retaining a very heavy stain. They sometimes show terminal budding (Fig. 38) or traces thereof.

In a few cases a large race or species has been found which is more resistant to iodin-eosin, simulating in size and form the ellipsoidal small race of *E. nana* and *E. dysenteriae* (Fig. 35). These float off on concentration and reveal their affinities to the yeasts in stained preparations.

FECAL MOLDS

On stools which have stood for a day before examination, there may appear a gray coat of mold (Fig. 43), some of whose spores are confusingly similar to protozoan cysts at first glance. They are, how-

ever, more highly refractive, have heavier walls, and are often more vacuolated. An examination of the surface coating of the stool will reveal the source. The range in diameter is from 7 to 15 microns and in form from spherical to ellipsoidal, or somewhat quadrangular, and they are sometimes accompanied by elongated cylindrical sections of the hyphae. Small spherical forms found with these molds are distinguished from *E. dysenteriae* by higher refractivity, heavier cyst walls and absence of typical nuclei.

There occur erratically in stools, often abundantly, certain peculiar cysts (Fig. 34) of unknown affinities. They are about 10 microns in length, broadly ovoidal, truncate at the smaller pole, with thick-walled cyst except over the truncate area. The cytoplasm shows an axial, granular zone and central nucleus with karyosome. They are frequently enveloped in a fibrous, indefinite sheath.

It should be noted, in closing, that repeated successive examinations are essential to establish an adequate diagnosis and that flagellate infections are most readily detected in fluid stools after a saline purge, whereas the encysted phases of these and of the entamebas are more readily found in the formed stools of infected persons. The intermittent or rhythmic appearance of the encysted phases of the intestinal protozoa necessitates these repeated examinations to detect infections. Three successive examinations will detect the majority of infections revealed by cysts, and six may be considered to indicate a probable negative. Repeated examinations at intervals of several weeks are desirable in critical cases. All tests of cure after treatment should rest only on several repeated series of examinations to be conclusive.

THE IRRITABLE HEART IN GENERAL PRACTICE

A COMPARISON BETWEEN IT AND THE IRRITABLE HEART OF SOLDIERS *

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During the last year or two medical literature abounds with various descriptions of the soldier's and recruit's heart. Indeed, so much has been written that with but a superficial knowledge or interest in cardiology, the impression is gained that a new and distinct entity characteristic of warfare had been discovered, and that it is never, or only extremely rarely, observed in civil life. This impression is heightened by the fact that similar conditions in civil life have scarcely been alluded to in the numerous reports, and that new and more or less confusing names have been given to this complex. To mention a few: The soldier's heart; effort syndrome; neurocirculatory asthenia; neurocirculatory myasthenia; disordered heart action and hyperthyroidism. From the broader viewpoint of clinical medicine, and as a result of an intensive study of the condition in cardiologic practice for many years, the examination of hundreds of candidates before the draft board, and a brief observation in camp hospitals, I believe the term "irritable heart," or even "cardiac neurosis" best fits the syndrome. Either appellation applies to all types of instability and irritability of cardiac innervation both in general and military practice in which there are assumed to be no organic cardiovascular changes. These terms, irritable heart and cardiac neurosis, are admittedly generic. They should be so, I believe, because the condition may have different underlying etiologic factors and varying clinical manifestations.

Perhaps, because of the early intensive cardiologic work in the present war, the fundamental relationship between the irritable "soldier's" heart and a similar condition in civil life has not been emphasized sufficiently. Various theories were at first propounded to explain its frequency in soldiers. For example, infection was assumed to play a fundamental rôle.[1] But the numerous cases occurring in American camps among recruits who had never seen active service and who had had no infection tended to upset this theory. The fact that

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* Read in part before the New York County Medical Society, April, 1919.

1. Medical Research Committee, Special Report Series No. 8, 1917, Report upon soldiers returned as cases of "Disordered Heart Action" (D. H. A.) or "Valvular Disease of the Heart" (V. D. H.).

diminished blood alkalinity (acidosis) was found in a certain number of the cases studied abroad, was also given as a tentative explanation. It seems possible that in such individuals the "acidosis" and change in the buffer salts in the blood[1] may have been the result instead of the cause of the irritable heart because of the circulatory disturbance and consequent interference with proper elimination of toxic products.

Intensive military training has taken men from civil life without regard to their previous occupations, and has immediattely exposed them to the stress, exertion and fatigue of camp life. I am not criticizing this procedure, because the exigencies of the war undoubtedly demanded haste. Besides, it may perhaps have been wise to discover as soon as possible those recruits who were totally unfit for actual war service. Concomitant with unwonted muscular exertion, especially in those from sedentary life, there is a certain amount of nerve fatigue, perhaps best expressed by the common term "fag." Nerve fatigue, psychasthenia and neurasthenia, are admittedly somewhat vague terms and are open to wide variances in meaning, but they best express a tendency to quick exhaustion, inability to properly coordinate somatic and even cerebral functions, and irritability and restiveness of these functions. This nerve fatigue and instability often characterize patients with irritable hearts. In addition, there is the important emotional factor, the mental attitude of the recruit toward war. Is he cowardly by nature? Does he fear warfare? Can the natural diffidence against war in a peaceloving people be overcome rapidly enough by instillation of the martial spirit, of military morale? Can the recruit's mind readjust itself rapidly enough to the vital necessity of risking life and limb for country? How far are such questions related to the nerve stamina of the individual? Does the recruit come of nervous stock? Has he shown any neurotic manifestations in civil life? Have venery and sex ideas played a large share in his thoughts? Questions like these undoubtedly play large rôles in the mental and nerve poise of the individual, may retard or induce, considerably influence, or even cause the advent of the irritable heart.

Such are some of the important crass neurologic and psychiatric factors in camp training. These are tremendously intensified by actual warfare and combat; the nerve tension, perhaps of weeks, before actual combat; the dread of injury or death in the clash of batttle; the nerve exhaustion following it; fright in all its phases; these are here the outstanding factors.

Is there any correlation between the irritable heart under camp and war conditions, and that found in general practice? I believe the two conditions are comparable, and that its infrequency in civil life is due to the relative rarity of the factors just mentioned. Besides,

in general practice, I believe we do not delve sufficiently into possible etiologic data. We are prone to weigh the patient's story too lightly because there is no tangible corroborative physical evidence to be seen, heard or felt. Neurotic individuals, especially those with cardiac neurosis, have frequently told me that they feel anger and excitement "in the heart," while others with gastric disturbances feel similar emotions "in the stomach." It may appear unscientific to believe such statements when no method of examination is open to us to prove or disprove them, but, measured by our own personal experiences, I am sure that there are physicians who at some time, under special emotional stress, such as fright and anger, have referred their sensations to the heart or abdomen, and I need but recall poetic and romantic literature which abounds with examples of pangs of jealousy and rage being referred to the heart.

I shall now give a few examples typifying the irritable heart as observed in general practice, and shall emphasize particularly the probable underlying neurologic "insult" which initiated cardiac symptoms.

REPORT OF CASES

CASE 1.—J. F., aged 28, a furnace worker for years and a man of strong muscular development, had been married five months. The only infectious disease he can remember is typhoid when a child. Although continually at his laborious work, he had had slight precordial pains for some months. He cannot account for their origin. Three weeks ago, he had a quarrel with another laborer. Since then he has had a dry cough, and occasional palpitation and dyspnea. The patient has lost 13 pounds in weight since the onset of his illness.

Examination.—The lungs are normal. Inspection of the precordium reveals slight overaction in the mitral area. There is no precordial sensitiveness on slight or deep pressure. On auscultation there is heard a strong ventricular apical impact; the first sound is somewhat like a thrill and split in character. The other sounds are normal. The pulse rate varies suddenly from 72 to 100 per minute. This increase is not always caused by exercise. When the heart beats at the higher rate, it can be slowed considerably by having the patient take a deep breath and holding it for several seconds. The thyroid is not enlarged. The systolic blood pressure is 142; the diastolic, 70. The urine is normal. There is no edema of the legs. The knee reflexes are very lively. The cardiac outlines, as shown by the orthodiagram, are normal; the fluoroscope shows definite overaction of the aorta and pulmonary artery.

This patient presented no evidence of organic cardiovascular disease. A dispute with a fellow laborer had apparently aggravated a dormant cardioneurotic condition, and produced hyperexcitability of the cardiac nerve mechanism, with consequent sudden rapid rhythm and the uncomfortable sensation of palpitation. I advised the patient to give up his work for a week or two, not because I feared the effect of work upon his heart, but for purposes of mental rest and relaxation. Bromids in moderate amounts were also advised. I

have since heard from the family practitioner that the patient followed directions and that he is again at work and feeling well.

CASE 2.—J. R., aged 27, unmarried, a grocer, stated that he had had occasional precordial discomfort in lifting heavy boxes. This, however, never interfered with his activities until five years ago. He then had an attack of severe abdominal colic and felt faint. His heart action became rapid. The doctor who treated him at that time stated that the heart action was regular, the rate 180 per minute. Since then, any excitement, undue mental strain, attempts at hard work, or even full and hearty meals are accompanied by rapid heart action and precordial pains. His appetite is good, he has not lost weight. He has become introspective about his heart, the more so since he has been drafted and accepted for military service. There is no history of any previous infection.

Examination.—The patient is robust and well nourished. The thyroid is not palpable. The systolic blood pressure is 110; the diastolic, 90. Inspection of the chest reveals slight apical overaction. On palpation, there is a thrill-like systolic shock at the apex. There is no precordial pain or sensitiveness to superficial or deep pressure. At the apex, the first sound is strong and is so broken up or split as to give the impression of a thrill; the other cardiac sounds are normal. The orthodiascopic tracing shows a somewhat enlarged pulmonary artery; the other cardiac curves are normal in shape and size. The abdominal examination presents nothing abnormal. There is no edema of the legs. The urine is normal. The knee reflexes are somewhat exaggerated. When at rest, the pulse rate is 100 per minute; the rhythm is normal. After moderate exercise—for example, walking 100 feet fairly rapidly—the rate rises to 150 per minute; the patient then complains of some dyspnea and precordial distress. After three minutes rest, the pulse rate returns to its previous level.

The original "insult" was an attack of paroxysmal tachycardia following severe abdominal colic. Prior to that, he was a hard working individual whose only complaint was the not unusual one of precordial distress from heavy lifting. The original paroxysm of tachycardia has left the cardiac mechanism hyperirritable, so that undue excitement or moderate physical exertion caused rapid heart action with dyspnea and precordial pain. Despite the physical signs over the mitral area on palpation and auscultation, I believe that organic disease can be excluded. I have found identical signs, a thrill-like broken systolic shock on palpation, and a thrill-like broken and strong systolic first sound in a number of recruits of the draft age in whom, after exercise, cardiac action was accelerated or over-forceful.[2] Such abnormal signs are not evidence of organic disease in these individuals, for when the cardiac rate or overactivity can be controlled, as, for example, by having the patient breathe slowly and deeply, the abnormal signs become less marked or even disappear. There was nothing in the patient's previous history, neither rheumatism nor other infection, which could be correlated etiologically with pathologic damage to the heart.

2. Neuhof, S.: Cardiovascular Examinations of Draft Candidates by the Local Boards, N. Y. Med. J. **107**:411, 1918.

CASE 3.—L. R., aged 48, married, salesman, has always been very active and athletic, but of neurotic temperament. He had palpitation when 20 years old. He frequently suffers from cold hands and feet. For several months he has had frequent quarrels with his wife. The chief cardiac symptoms are sudden, momentary palpitation, especially at night, and clammy hands and feet. He is now afraid to exercise because he believes he has heart trouble. He never has any dyspnea while at his work. His family physician states that he has an occasional dropped beat (extrasystole) and that he has an occasional hyaline cast in the urine.

Examination.—The man is of athletic build. The systolic blood pressure is 118; the diastolic, 95. His hands and feet are cold, clammy and wet with perspiration. The pulse is regular; the rate, normal. The heart sounds are normal. There is no precordial sensitiveness. Rapid walking does not abnormally increase the cardiac rate; after two minutes rest, the rate reaches the normal. The orthodiascopic tracing shows an aorta of normal size and contour. The heart is not abnormally large for a man of his physique. The knee jerks are lively. There is no edema of the legs. The urine contained no albumin, sugar or casts. Although there was no arrhythmia during the examination, the physician's observation and the patient's statement make it probable that the "palpitation" is due to occasional extrasystoles. The instability of the vasomotor system—sweating and clammy extremities—was the most prominent phenomenon.

The etiology of the cardiac and vasomotor symptoms was quite evident, family nagging in a neurotic individual. This fact also accounted for the attacks at night. During the day his mind was occupied with his work; in the evening and at night came the irritation and time for introspection. The etiology naturally suggested the remedy. First, the absolute assurance to the patient that his heart was normal. As proof of this he was advised to continue his athletics and business. Second, avoidance of family quarrels. The patient was also given 30 grains of mixed bromids at night and 5 grain of the extract of suprarenal gland, the latter to be taken when the vasomotor and cardiac symptoms were particularly prominent. The attack ceased after several days; he was soon able to take up his business and athletic activities.

CASE 4.—H. M., aged 26, unmarried, theatrical manager, gives a questionable history of rheumatism in childhood. His mother has hypertension and is extremely neurotic. As a college student he had always been well, was fond of athletics and never had any cardiac symptoms until five years ago. He was then a helpless eye witness to the drowning of his brother. He became hysterical and was confined to bed for two weeks with hysterical attacks. Soon thereafter, and for two or three years, he had nervous indigestion; the chief symptom was belching. The gastric condition improved under treatment. He then developed cardiac symptoms; these consisted of palpitation and of pain in the left chest, particularly after excitement. After walking a mile now, he becomes "tired all over." He has recently been told by a physician that his heart is occasionally irregular. He is a very rapid eater. His business as theatrical manager leaves him no time for relaxation.

Examination.—The thyroid gland is not enlarged. The systolic blood pressure is 120; the diastolic, 60. There is slight carotid hyperactivity and slight exaggeration of the apical impulse. The sounds at the base are normal. The first sound at the apex is normal; it is immediately followed by a sharp, super-

ficial click which is transmitted somewhat to the left; it disappears on deep inspiration. There is an occasional superficial pleuropericardial rub to be heard in this region. There is no precordial sensitiveness. The pulse rate is normal; rapid walking produces no dyspnea and only slight acceleration of the cardiac rate. The orthodiascopic tracing shows a heart of normal size and contour, the ventricular contractions are very vigorous. The examination of the abdomen presents nothing abnormal. There is no edema of the legs. The knee reflexes are very lively.

I believe that the adventitious sounds at the apex are due to an old pleuropericarditis and have no relation to the patient's symptoms. The demeanor and action of the patient during the examination were those of an individual who is hyperactive and excitable. Whether this nervous instability antedated his brother's drowning, or whether the latter only intensified an inherent tendency, I cannot state because of insufficient data regarding his early life. The history leaves no doubt that the original hysterical attack was the starting point of a train of nervous symptoms which first affected the stomach and later the heart, producing the subjective feeling of palpitation and precordial discomfort. The symptoms were present despite the fact that the cardiac rate was normal and was not inordinately increased by exercise; this phase of the symptomatology will be discussed later.

The question arises, would such a patient make a good soldier? I do not believe that the pleuropericardial sound should invalidate him from military duty. Since there is no tachycardia following effort, the fundamental question is the psychologic one of his attitude toward the war. If properly patriotic, camp life with its release from the type of hurried and harried life he had been leading, would probably cause a trend toward a normal, physiologic level, and his cardiac symptoms would cease. I have since heard that he entered the army and developed no further cardiac symptoms.

To show that the irritable heart in women may resemble those found in men, I have added the following two cases:

CASE 5.—Mrs. W., aged 52, has had five children and several miscarriages. The menopause occurred two years ago. At that time she had occasional slight flushes for two months. Ten years ago she had gallstone attacks for which she was treated in Carlsbad. She has had no attacks for several years. Her husband died suddenly in bed two years ago. She was very much upset by his unexpected death. Since then she began to have palpitation, especially at night, and dreaded going to bed for fear that she too might die suddenly. She also had palpitation when excited or when walking in the street. This was accompanied by sharp substernal pain, which occasionally radiated to the left arm. The systolic blood pressure taken at different times varied between 180 and 200. She had been told that she has, and she has been treated for, hypertension and arteriosclerosis. She had been on a rigorous diet; and although often hungry, accompanied by faintness and tachycardia, she was afraid to eat because of the fear of increasing the blood pressure.

Examination.—The patient, a stout woman, is not dyspneic while at rest. The thyroid gland is not enlarged. The systolic blood pressure is 150, the diastolic 100. There is some overaction of the carotids and aorta. There is no pain on superficial or deep precordial palpation. There is a strong systolic impact felt at the apex. On auscultation all the cardiac sounds are normal. There are no murmurs or accentuated sounds. When at rest, the cardiac rate is 110; it is slightly decreased on deep quiet inspiration. Walking causes a cardiac rate of 120 per minute; after a few minutes, it drops to 110. There is no edema of the legs. The urine and knee reflexes are normal. The orthodiascopic tracing shows a heart of normal size and form. The electrocardiogram shows nothing abnormal.

In spite of the history of hypertension and of precordial attacks, I regarded the case as one of pure cardiac neurosis due to fright, reflexly aggravated by hunger pangs; the latter was due to a starvation diet which kept the stomach empty a good part of the time, and probably induced gastric hyperperistalsis. I allowed the patient a liberal, mixed diet, to be eaten at regular intervals. She was given bromids at night, and 5 grain tablets of the extract of suprarenal gland for the attacks of tachycardia. Within three weeks her condition improved remarkably. The systolic blood pressure was 130; the precordial pains disappeared; the cardiac rate fell to 80 per minute. The patient slept well at night. She walked regularly in the open without discomfort. Reassurance doubtless was a large factor in the improvement.

Case 6.—Mrs. G., aged 26, has been married one year. She has a baby three months old. Seven years ago she had a love affair; she became disappointed in her lover and gave him up. She then had many hysterical spells, finally culminating in attacks of severe nocturnal dyspnea. Since then she has had many such attacks. While pregnant the attacks ceased entirely, but they have recurred recently. Her home life is a happy and comfortable one. During a typical attack, her hands and feet become cold; the heart action, rapid; she becomes dyspneic, there is a feeling of palpitation and of abdominal pressure; accompanying the latter is intestinal hypermotility and rumbling. The patient says she tries to control the attacks, which usually come on and are severest at night. She is losing weight and fears going out because of the attacks. Her appetite is poor.

Examination.—The teeth and tonsils are normal, the thyroid not enlarged. During the examination, her hands become cold and clammy. The patient stated that she was having a mild attack. Inspection of the cardiac area was normal. There was a broken, thrill-like systolic shock palpable and a thrill-like first sound heard over the mitral area. The other heart sounds were normal. The cardiac rate was 110 per minute; slight exercise (walking in the room) brought the rate to 120 per minute. At the end of the examination, the rate was 100 per minute. The abdomen presented nothing abnormal. The knee reflexes were very lively. There was no edema of the legs. The orthodiascopic tracing showed a heart normal in size and shape.

This is an excellent example of a heart made irritable originally because of an emotional strain sustained years ago. The symptoms subsided during pregnancy, apparently because the pregnant state caused a profound change in her mental attitude, a common result

of pregnancy. A hyperfunction of one or more of the endocrine glands may have been the fundamental cause of such change. After pregnancy, there was a recurrence of the old symptoms, vasomotor instability and dyspnea were the chief of these. Rapid heart action in itself can cause dyspnea. The presence of vasomotor symptoms, due to irritability of that center, seems to indicate in addition the possibility of hyperexcitability of the respiratory center. Studied with a respiratory apparatus such patients may be found to be suffering from tachypnea, rather than from dyspnea.

A review of the few examples given, as well as of the vast majority reported in the literature, shows that the salient feature of the symptom complex of the irritable heart has been instability of the vasomotor or of the accelerator mechanism, or of both. I believe that all the symptoms, as well as the abnormal physical signs, are derived from these fundamental disturbances. Giddiness, flushes, pallor, dermatographia, swooning, fainting are evidently due to vasomotor disturbances. They are found very frequently, for example, in many types of gastric disorder without cardiac symptoms. The tachycardia in irritable heart ranges from simple pulse acceleration to gradual or sudden, sharp increases in rate following exercise, emotion or unknown causes. To use a simile derived from physiology, the threshold for the abnormal excitation varies considerably. The cause of the various types and degrees of precordial sensation, such as heaviness, pressure, pain, skin and deep sensitiveness, is still obscure because nerves of sensation have not been discovered in the heart and the reflex arcs involved are still matters of surmise. But the clinical fact, already alluded to, that some people in anger or fright refer the first sensation to the heart, and Head's theory of sensitized spinal segments, indicate how a diseased or improperly functionating organ can cause various local referred sensations.

The abnormal physical sign of irritable heart to which most importance is attached, is a thrill-like palpable systolic impulse and the thrill-like, split, or broken first sound at the apex. Soft apical murmurs that are not transmitted, slightly accentuated second pulmonic sounds, and the occasional reduplicated second sound over the pulmonary artery, the aorta or at the apex, may be dismissed because they are not characteristic of the irritable heart and are sufficiently common in other conditions. When present, the thrill in the irritable heart with tachycardia is systolic in time; its degree and transmission seem to depend on the violence as well as the rapidity of the heart action. A thrill, for example, is infrequent in the rapid regular heart action of paroxysmal tachycardia, in which the heart beats at the rate of from 150 to 200 per minute. It is quite common, however,

in exopthalmic goiter, even when the cardiac rate is as low as 100 to 110 per minute. I believe it is the violence of the heart action, rather than its rapidity, that accounts for the abnormal systolic thrill, for theoretically, at least, it seems probable that blood, suddenly and forcefully ejected by ventricular systole, can produce impinging countercurrents and whorls against the inner ventricular surface, which, to the ear and touch, are interpreted as broken, almost cog-tooth-like interruptions of the normal systolic sound and thrust. This receives some support from the observation I have frequently made that if the cardiac rate and hyperactivity can be controlled, as is frequently the case, by having the patient take a long, deep breath and holding it a moment, the thrill often diminishes or disappears, almost commensurate with corresponding decrease in ventricular hyperactivity.

I believe I have shown a close etiologic and symptomatic relationship between the irritable heart in general and military practice. In the latter, tachycardia, especially following effort, is the most common sign; vasomotor symptoms alone are less common, while in general practice, the vasomotor symptoms often predominate. It must be remembered and emphasized that patients frequently complain of palpitation without tachycardia, that is, they have a subjective feeling of palpitation. In a few instances, I have been able to discover with the aid of the fluoroscope that such patients showed particularly strong ventricular contractions; the left ventricle was decidedly diminished in size with each systole. This may perhaps be the physical explanation of subjective palpitation in some of these cases.

I have tabulated a list of the commoner symptoms, physical findings and etiologic factors as I have observed them in the neurotic heart in general practice, and have arranged each column, as far as possible, in the order of the importance of the various factors.

IRRITABLE HEART IN GENERAL PRACTICE

Symptoms	Physical Findings
Abnormal precordial sensations (pain, sensitiveness, oppression)	Normal sized heart; thrill-like, split systolic impact and first sound over the mitral area
Vasomotor symptoms (giddiness, flushes, dermatographia, faintness)	Systolic murmur over lower precordium; rapid regular heart
Dyspnea (actual and subjective).....	Normal rate with occasional extrasystoles
Extrasystoles producing subjective sensations	Sudden changes of heart rate
Tachycardia following slight effort.....	Slow heart action with powerful ventricular contractions
Constant tachycardia	
Sudden changes of heart rate	

Etiologic Factors	Therapy
(Causing hyperirritability of the sympathetic system):	Reassurance
Previous history of shock, fright or emotional strain	Short rest
Reflex excitation from gastro-intestinal canal.	Retraining, especially through graded games
Physical fatigue with insufficient rest.....	Bromids in the beginning or in severe cases
Insufficient recuperation following acute infections	Suprarenal gland extract (especially for vasomotor symptoms)
Disturbance of the organs of internal secretions (thyroid? adrenals?)	

Some of the headings require additional comment; others have been discussed in the description of the case histories or otherwise.

Dyspnea, as stated, may be actual, e. g., in patients who develop tachycardia as the result of exercise. At other times, especially in patients with vasomotor symptoms, the dyspnea seems purely subjective, for there is no increase in the rate or depth of the respiration. In rare instances, tachypnea — rapid breathing — results.

The size of the heart, as mapped out by ordinary methods of clinical examination, gives the impression of enlargement. This impression, however, is the usual one in almost all cases of violent, rapid heart action. I have had occasion to fluoroscope many cases of tachycardia that had no organic cardiac disease. In every instance, I made orthodioscopic tracings, an exact method of delimiting the cardiac area, and I was not able to demonstrate any characteristic change from the normal in the size or configuration of the heart. I have not measured the breadth or other cardiac diameters according to the somewhat popular standards of Dietlin and Groedel, because these standards apply chiefly to those of normal physique. This physique approximates the normal in soldiers, hence standardized measurements may be of some value in them. But I have frequently found the standard (a transverse diameter of 11 to 13 centimeters) too small, especially in those whose diaphragms are high and not very mobile. In these individuals, the ventricular surface lies abnormally flat along a disproportionate part of its length, hence the resultant breadth is larger than the standard, although the organ is not actually enlarged. On the other hand, I have only rarely found the drop or pendulous heart, that is, a narrow organ resting lightly on the diaphragm along a small part of its under surface.

Among etiologic factors of the irritable heart, I have mentioned, as a fundamental factor, an "emotionally unstable, neurotic individual" (see table). Some of the patients give definite histories of a nervous taint in either parent, or in a closely related member of the family. I believe, however, that while such taints may be common, they are not the actual exciting or impelling causes of the neurotic heart. Some great emotion, fright, dread, shock, is usually the directly antecedent cause of the outbreak of the cardiac symptoms. Reflex excitation from the gastro-intestinal canal is the next most frequent. In other words, the cardiac nerves of an hereditary neurotic individual apparently react more readily, more continuously and in a more exaggerated fashion to a neurogenic "insult" than do those of an individual with normal poise.

CAUSE OF IRRITABLE HEART

Having described some illustrative cases and sketched various symptoms, physical findings and etiologic factors, the question arises is there some basic underlying excitation to account for the irritable heart? Careful analysis of all the various phases of the irritable heart, especially facts elicited by a careful history, lead me to the belief that it is probably fundamentally due to hyperexcitation of the sympathetic nervous system. In his classic paper on the irritable heart of soldiers, Da Costa[3] ascribes many of the symptoms to stimulation of the sympathetic system. Recent observations of the same subject show that there exists hyperirritability of the accelerator reflex arc[4] and probably also of the vasomotor mechanism.[5] No diminution of the vagal tone was found, as judged by atropin experiments. Experimental observation demonstrates that fear and dread in cats, for example, is accompanied by erection of the fur, by exceedingly rapid heart action, by profuse perspiration and by staring eyes. These are all apparently due to hyperexcitation of the sympathetics. Such symptoms have their analogies in man. Fright and terror can be the immediate cause of exophthalmic goiter. Authentic cases of this type have been reported. I myself have observed at least two such undoubted cases. One of these was that of a young girl, who, while riding in a passenger elevator, saw a man killed before her eyes. On reaching home, she went to bed with rapid heart action, and within a few weeks, developed all the classical signs of exophthalmic goiter. In recruits, the development of typical exophthalmic goiter has been observed occasionally. On the other hand, the development of rapid heart action, tremor and the other signs and symptoms of the irritable heart, without the type of goiter found in exophthalmic goiter, has been regarded by some as evidence of hyperthyroidism.[6] Some of these individuals had soft goiters. But changes in the thyroid, especially cystic degenerations, are by no means accompanied regularly by cardiac or nervous symptoms. The subject of hyperthyroidism brings up for discussion the moot and involved question of the endocrine glands. Are we justified in assuming hyperthyroid activity without the typical eye and thyroid signs of exophthalmic goiter? I do not believe that the present state of our knowledge allows us to go thus far. Besides, I think that the symptoms of hyperthyroidism,

3. Am. J. Med. Sc., January, 1871, p. 40.
4. Cotton, Rapport and Lewis: Observation on Atropin, Heart **6**:295, 1917.
5. Cotton, Slade and Lewis: Observation on Pilocarpin Nitrate, Heart **6**: 299, 310, 1917.
6. Brooks, H.: Hyperthyroidism in the Recruit, Am. J. Med. Sc. **156**: 726, 1918.

so-called, can be understood better and more rationally on the broader and more fundamental basis of hyperirritability of the sympathetic system. It is possible that this supposition may even explain why some cases of irritable heart develop all the classical signs of actual exophthalmic goiter, for the endocrine glands themselves, especially those endowed with a rich nerve supply, are presumably subject to varying influences of nerve excitation and tone. This has been proven experimentally for the suprarenals. The entire subject is further complicated by the probability that the endocrines themselves are mutually influenced through the action of hormones. This was illustrated in a case I saw at one of the camps in which the development of a constant tachycardia was one of the prominent features. The man had gained about 50 pounds in weight within a few weeks; his breasts had taken on female characteristics and sexual desire had disappeared entirely for several months. The thyroid was not enlarged; there was no exopthalmos nor tremor. Despite the rapid heart action, he looked the typical example of hypopituitarism. According to the present terminology, the case would probably be classed as dyspituitarism.

Hyperexcitation of the sympathetic system can undoubtedly produce rapid heart action, tremors and sweating; and, as already stated, symptoms starting thus, may, in some instances, finally eventuate in actual exophthalmic goiter. In several polygraphic tracings of undoubted cases of exophthalmic goiter, I observed that the conduction time from auricle to ventricle (the *a-c* interval) was diminished even when tachycardia was not marked.[7] This fact may offer some clinical corroboration of the experimental observation[8] that one of the effects of stimulation of the sympathetic is a decrease of this interval. Only recently[9] it was pointed out that the thyroid is subject not only to hyper- and hypo-, but also to dysfunctions, a fact which may account for some of the vagaries and apparent contradictions in the clinical syndrome of exophthalmic goiter.

The physiologic antagonism between the sympathetic and vagus systems, between the accelerators and inhibitors is, of course, well known. In an abnormal antagonism between these two controls, I believe that even when inhibition is normal, its power can be nullified by hyperirritable and hyperactive accelerators. In other words, the inhibitory tone, as tested by atropin, may be normal, yet its power

7. Neuhof, S.: Clinical Cardiology, pp. 55, 104.
8. Rothberger, C. J., and Winterberg, H.: Ueber die Beziehungen der Herznerfen zur Form des Electrocardiograms, Arch. f. d. ges. Physiol. **135**: 506, 1910.
9. Janney: Arch. Int. Med. **22**:187, 1918.

can be nullified by hypertonic accelerators. This is perhaps explicable by the physiological fact that, tested electrically, there is normally no quantitative relationship between these two systems. Sympathetic hyperexcitation, therefore, can apparently upset the nice balance of cardiac nerve control, with consequent instability or lack of the normal inhibitory process.

May we not, therefore, infer that the irritable heart is due fundamentally to sympathetic hyperexcitation, unopposed or insufficiently opposed by the inhibitory apparatus, and that therefrom arises the cardiac syndrome, with vasomotor symptoms, mild tachycardias and palpitation, with and without effort, as one extreme, and the actual goiterous heart at the other?

The fact I wish to emphasize is that the soldier's irritable heart is no new complex, but is the same syndrome seen in civil life, intensified and multiplied by training and war conditions. Suspense and fright intensify latent and dormant symptoms and tendencies and cause nervous instability in those temperamentally unfit, by heredity or otherwise, to "carry on."

The treatment abroad of the soldier's heart had narrowed itself to a comparatively short period of rest and then graded restraining in camp routine, mild exercise at first, route marches, light packs, heavy packs, etc. In this way a fair percentage of these soldiers become fit for active duty. Digitalis was not found to be of any value, as indeed was to be expected, for the patient did not suffer from decompensation, nor was there any evidence of organic, valvular or muscular disease. At the beginning there had been no attempt to attack the problem of the irritable heart from the psychologic or psychotherapeutic viewpoint. Mental and physical relaxation, especially in the form of games, and later sports, was not then attempted. More recently, especially in the United States, games and farming have been used therapeutically. In private practice, where these matters can be individualized better, I have found that, if after a careful examination, patients could be assured that they had no heart disease, and that all the symptoms were the result of "upset nerves," the cure was tremendously hastened. An explanation, especially to intelligent patients, which is not too scientific, but which offers a sufficient cause for the symptoms, is also of distinct benefit. What patients dread most is sudden death; with a satisfactory explanation for their symptoms, they are usually relieved, sometimes permanently, of this fear. For the purpose of mental relaxation, as well as gradually increasing the amount of exercises, I have suggested billiards, croquet, bowling, golfing, light farming and, in cases that are improving, rowing and even swimming in shallow water. Reeducation of the tone of the

cardiac nerves in order to regain stability is ofttimes a slow and tedious process. Sudden sharp exercises should be avoided. The doctor should never omit praise, even exaggerated praise, for good work done on the patient's part in overcoming his timidity to exercise, and especially in continuing exercise and play, despite the presence of minor symptoms, such as moderate tachycardia and slight precordial pain.

Medicinally, I have found mixed bromids and suprarenal gland extracts the best drugs. The bromids given in large doses at first, lessen mental irritability and anxiety. My usual procedure is to give 1 gram of the mixed bromids, well diluted in water, three times a day after meals. Depending on the progress of the case, the dose is correspondingly diminished and finally stopped. In cases that are annoyed by sleeplessness, I add 10 grains of chloral hydrate or 8 grains of veronal every night for a few nights. I have seen no bad effects on the heart or the individual from these procedures. The suprarenal gland I prescribe in 5 grain tablets, to be taken only when symptoms, such as tachycardia or precordial distress become annoying. Paradoxical as it may seem, I prescribe this extract even when hypertension is present. Its beneficial effect seems to depend on its power to stabilize temporarily and decrease vasomotor instability by its action on the vasomotor center; it thus counteracts the cause of many of the symptoms. The effect of the drug is only temporary, hence with recurrence of the symptoms, the dose may be repeated, if necessary, several times a day.

SUMMARY AND CONCLUSIONS

The irritable heart as observed in general practice is similar to that found in soldiers. Vasomotor symptoms are more pronounced in the former. The etiologic factors are similar, but because of training and war conditions, rmant and latent neuroses crop out oftener and are more readily evoked; consequently the cardiac syndrome is more violent and lasts longer. Infection is a factor only in so far as it induces and produces nerve and muscular fatigue and psychasthenia. There is no pathologic change in the cardiovascular system. The fundamental cause of the cardiac neurosis with its various manifestations, seems due to hyperexcitation of the sympathetic nervous system.

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DURATION OF NORMAL CONVALESCENCE

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These notes on the duration of normal convalescence are the result of work that was primarily designed for the treatment of war casualties, especially those resulting from gas inhalation. It was hoped to reduce the period of convalescence for gas cases and to avoid the relative frequency of effort syndrome so conspicuous in the British army. In reviewing the first five thousand case histories, which are to be the basis of a report on the functions of convalescent camps, a sufficient number of different cases were found to warrant deductions and suggestions as to the optimum duration of the convalescence from peace time surgical and medical affections. Many of the neurasthenias and anxiety neuroses follow operations or acute infections, where the patient is allowed to return to the wear and tear of the usual activities of life after a relatively short period. It may well be that the prolongation of convalescence, with graduated exercises, which proved so beneficial in the case of physical injuries, will minimize the exposure to psychic trauma during that period, and thereby prevent the outspoken mental symptoms which are apt to follow, especially in those individuals whose psychic resistance is below the normal. The daily life of soldiers subjects them to strain and to labor more intense than that to which civilians are commonly exposed, so that the recovery to normal demands the attainment of a higher standard than is sought in civilian practice. However, one is concerned with the recovery of what was lost by sickness, and in that sense the results are comparable with peace time conditions.

The camp in question was the convalescent section of a group of base hospitals which had a total capacity of fifteen thousand beds, the camp maintaining two thousand patients. These hospitals were about 50 miles from the front, and, in times of stress, became evacuation centers where patients stayed but a few days on their way further back. But in the main, the soldiers, especially those with complaints such as are met with in daily life, were treated and then discharged to duty, reclassified, or sent to the camp for convalescence or protracted observation.

The underlying principle of the camp was the retraining, by graduated exercises, of soldiers who were on their way back to the front lines — a training point and not a hospital. It was essential to insist on military discipline in order that the men, on their discharge, should be mentally, as well as physically, qualified for their normal duties. A suitable amount of relaxation was afforded by games, moving pic-

tures, theatricals, etc., which filled up practically all the time not devoted to the setting-up exercises, squad drills, hikes and fatigues — the whole being under medical supervision. The food was consistently good and abundant, and the sleeping accommodations were fair — tents for the most part, well drained and with canvas floors. The work was done during the past summer and fall, so that no allowance need be made for the cold of winter. In general, the convalescence of the patients was favored by the local conditions.

On admission and discharge, a physical examination of the stripped patient was made in all instances, and promotion through the three classes, representing increasing physical demands, was dependent on the ability of the soldier to perform the work and play of the particular class without untoward symptoms. A small but satisfactory camp hospital, with access to the laboratory of the center, made possible a careful study of the individual during his stay.

The first qualification for discharge to full duty was the promotion of the patient through the two earlier and easier classes and his ability to accomplish the daily class work of Company Three — forty minutes of steady setting-up exercises, an hour of squad drill and a 5-mile hike. If there were no contraindications, the patient was stripped and examined and then sent with his notes to the writer for a final check. How much better than the customary manner of feeling the pulse, palpating the wound, listening to the heart, telling the patient to be careful, and sending him from the ward to full duty! By the observation in the camp, his tolerance for exercise was known, and the patient himself knew what he could do.

A further very important point was realized at the camp. On discharge, the patient was fresh from drill and military discipline, which enabled him to rejoin his outfit and to take his normal place among his companions. He had recovered from the great loss of discipline that is bound to occur in the base hospital, and he had been led back into the normal routine of a soldier's life.

In order to confirm the results, a "follow-up" system was instituted. Letters of inquiry were sent to the different battalion medical officers two months after the soldier had been returned to his organization. (If the war had continued, a second letter would have followed after six months, and a third after a year.) The answers to these questions as to the patient's condition were most convincing. To date, about two thousand of these letters have been returned, thanks to the cooperation and interest of the regimental surgeons, and in more than 99 per cent. of the cases, the patients discharged to Class A, who had not been killed, wounded or gassed, were fulfilling their normal functions. And those reclassified to lower categories were doing the work of their grade.

In order that the duration of stay in camp might not be unnecessarily prolonged, all patients were seen daily, after their drill, by medical officers. Thus, men who were in good condition on entry to the camp were discharged three days after admission, the minimal time consistent with their promotion through the three classes.

To compare the duration of hospitalization of patients passing through the camp with those discharged directly to duty and not tested for their physical tolerance, a group of records was obtained from the hospital center of the period before the adoption of the convalescent camp, and before the rush of wounded and gassed necessitated rapid evacuation. These averages represent the periods which different physicians thought sufficient for recuperation. No follow-up system had been instituted for these patients, so that their final disposition is uncertain. But the writer, while working in a base hospital, has seen some of those discharged return to the hospital for relapse, weakness, painful wounds, or inability to keep up. In addition, after longer intervals, some of those previously discharged patients returned with functional mental disorders, whose precipitating trauma dated from their original entry. In the early method of handling patients, the initial stay in the hospital was sometimes proved to be insufficient, but as relapses were treated as new admissions, a false idea was obtained as to the total time lost. Transportation in France was always difficult and very slow, and any reduction in its use was well worth while.

The following tables show the average duration of stay in hospital and camps under the two systems. The first group, with the number of patients on which the average was computed, comprises those who were discharged to duty before the existence of the camp. The second group, with its larger number of cases, shows the number of days that the patients were in the hospital, plus their stay in camp. In this collection, cases complicated by secondary or intercurrent diseases are omitted.

In looking over these tables, certain suggestive observations can be made. In the first place, it is important to learn that in practically every type of disease studied, the period necessary for resumption of normal function is definitely longer than was allowed at the base hospitals.

The influenza group, which included slight colds, fever of a few days' duration, or malaise of sufficient intensity to warrant the evacuation of the patient from the front line, is the only one to show approximately equal periods. The majority of these soldiers were fit for duty on their arrival at camp, where three days were necessary for the completion of their course of work, so there is an apparent agreement in the two series. But attention should be called to a fact, not evident in dealing with averages, that a great many of the patients who came

TABLE 1.—Medical Conditions

Diagnosis	Number of Cases	Average Stay in Hospital, in Days, Patients Not Going to Camp	Number of Cases	Average Total Stay in Days in Hospital and Camp
Influenza	27	25	828	31
Pneumonia	24	35	170	58
Acute bronchitis	33	24	223	36
Mumps	20	18	53	39
Measles	0	0	18	27
Scarlet fever	8	57	7	77
Catarrhal jaundice	1	17	7	38
Diphtheria	0	0	5	57
Tonsillitis and sinusitis	34	19	90	34

TABLE 2.—Surgical Conditions

Diagnosis	Number of Cases	Average Stay in Hospital, in Days, Patients Not Going to Camp	Number of Cases	Average Total Stay in Days in Hospital and Camp
Hemorrhoidectomy	21	20	25	45
Herniotomy	31	24	41	50
Hydrocelotomy	6	22	7	54
Tonsillectomy	10	20	8	37

TABLE 3.—War Casualties

Diagnosis	Number of Cases	Average Stay in Hospital, in Days, Patients Not Going to Camp	Number of Cases	Average Total Stay in Days in Hospital and Camp
Gas	214	25	1,196	37
Enteritis	4	14	512	30
Concussion	6	25	102	45
Exhaustion	0	0	80	40

to the camp in the late fall, when true influenza was prevalent, were held in camp for long periods — two to four weeks — while their stay in the hospital had been only a few days. It was in this group that a great many of the effort syndrome cases were found, necessitating slow promotion. In all the other groups the figures make obvious the need for a much longer period of convalescence than was generally employed. It is interesting to learn the results in the infectious fevers. Physicians do not appreciate that the average case of mumps will not entirely have recovered until over five weeks after the onset of the disease, that the duration of the average pneumonia, including convalescence, will take over eight weeks, and scarlet fever over eleven weeks. Leaving out the possible relationship between the lack of proper care during the period of convalescence and psychic trauma, one cannot but consider the danger associated with a lowering of bodily resistance to other infections — to tuberculosis and to cardiac

infections, for instance. There may be some ground for the routine questioning of patients as to the infectious fevers of childhood, especially in the presence of an unexplained cardiac lesion, a mitral stenosis accidentally discovered, or a myocarditis without determinable etiology. May it not be that the frequency of these lesions might be materially reduced by a more careful treatment during convalescence?

Consider the group of tonsillitis and sinusitis. Most patients suffering from one of these infections are out of bed and back at their daily work after a week or ten days, whereas, in the case of these young soldiers who were in the best physical condition when they contracted the disease, it appears that the normal strength is regained only five weeks after the onset of the infection. Are we not, in our daily practice, taking risks greater than we have fancied? May not the neglect of proper care during convalescence be a source for development of more serious disease?

Similar reflections arise from a consideration of the records of surgical conditions. The average herniotomy needs several weeks of care before the patient is normal again, instead of the three and a half that are commonly allowed. So often one hears that some particular surgeon can get his patients who had simple cases of appendectomy out of bed and back to work in some phenomenally short time. Is that to his credit?

In the same way, it is conspicuous that the uncomplicated tonsillectomy requires over five weeks for complete convalescence. Certainly, the majority of patients do not allow themselves so long a vacation in general practice, nor do surgeons advise so long a period.

The results obtained seem definite as to the period required for complete convalescence. And it should be emphasized that the existence of a routine of graduated exercises and military discipline favored and hastened convalescence. It was the general rule that the patients clamored to get back to their organizations where their friends, accumulated pay and mail awaited them. For these reasons and from an acquaintance with the American "doughboy" it is hard to conceive that even a subconscious desire to remain out of the fighting could have protracted their convalescence in more than a very small percentage of cases. The medical supervision was real, and both the doctors and the ward masters soon became adept in handling the occasional malingerer.

This article is presented to the attention of physicians because it is believed to be the first direct attempt to employ actual physical tests for the determination of the optimum period of convalescence, and because the periods determined seem so much longer than are generally employed.

THE URIC ACID CONTENT OF THE BLOOD COMPARED WITH THE RENAL DIETARY TEST

THE BLAND DIET COMPARED WITH THE ORDINARY TEST DIET *

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During the past three years we have carried out about 180 renal dietary tests and blood analyses. Most of the cases were diagnosed nephritis or arteriosclerosis, though a number of other diseases have been included in the tables. The routine employed was as follows: The blood for analysis was collected before breakfast. The patients were in bed during the dietary test. They received a uniform quantity of water and food. In most instances the Mosenthal[1] modification of the Hedinger and Schlayer[2] diet was administered. The urine was collected in two hour periods from 8 a. m. to 8 p. m., and in one period from 8 p. m. to 8 a. m.

Recently Mosenthal[3] and Schlayer and Beckmann[4] compared the effect of a low protein or bland diet with that of the usual test diet. The former author found that both had approximately the same effect on the urine. Schlayer and Beckmann observed that in severe cases of nephritis the bland diet gave results which were similar to those obtained with the usual diet; in less severe cases the variability of the volume and specific gravity was more marked in the case of the bland diet, while in mild cases the difference between the two diets was even more striking. Their bland diet was administered in five meals. It consisted of a cup of milk and a roll at breakfast, a cup of milk and a roll in the forenoon; a plate of unsalted cereal soup and 500 to 600 grams of porridge at noon; a cup of milk and a roll in the afternoon and 500 to 600 grams of porridge and a cup of milk for supper. In our series of bland dietary tests the patients received 840 c.c. of milk, 45 grams of bread, 12 grams of oatmeal and 50 grams of rice divided into five meals. The nitrogen content of the diet was about 6 grams, the sodium chlorid content about 1.6 grams and the calorie value 890.

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* From the Department of Internal Medicine, State University of Iowa, Iowa City.

1. Mosenthal, H. O.: Arch. Int. Med., **16**:733, 1915.
2. Hedinger, M., and Schlayer: Deutsch. Arch. f. klin Med. **114**:120, 1914.
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TABLE 1.—Cases Showing a Moderate Abnormality in the Renal Dietary Test or Blood Analysis

Clinical Number	Age	Diagnosis	Blood Pressure	Heart	Edema	Albumin	Casts	Maximum Sp. Gr.	Variation Sp. Gr.	Night Urine		Blood	
										Volume, C.c.	Sp. Gr.	Urea N, Mg. per Cent.	Uric Acid, Mg. per Cent.
5735	27	Chronic interstitial nephritis..	180–110	+	—	+	+	1.015	9	567	1.015	23.4	4.7
		Same case.....	.....	..	..	..	..	1.020	4	515	1.019		
Obst.	17	Chronic interstitial nephritis...	492–120	—	—	—	—	1.009	4	750	1.009	19.6	3.1
3135	51	Chronic interstitial nephritis...	220–160	+	+	+	+	1.025	11	420	1.018	24.0	4.6
		Same case.....	.....	..	..	..	..	1.023	6	666	1.017		
3099	19	Chronic interstitial nephritis...	125– 83	+	+	+	+	1.020	0	900	1.020	17.4	
		Same case.....	.....	..	..	..	..	1.020	5	750	1.018	16.0	2.1
4978	20	Chronic interstitial nephritis...	170	—	—	—	—	1.014	3	745	1.014	18.9	2.0
4398	28	Chronic interstitial nephritis...	140– 90	+	—	+	+	1.035	9	124	1.030	31.0	4.1
4209	39	Chronic interstitial nephritis...	195–135	+	—	+	+	1.017	7	675	1.013	24.0	3.2
3484	24	Chronic interstitial nephritis...	120– 80	—	—	+	+	1.022	19	400	1.020	25.0	6.6
3294	64	Chronic interstitial nephritis...	270–170	—	—	—	—	1.020	13	280	1.020	15.6	5.0
5885	27	Chronic interstitial nephritis...	200–128	—	—	+	+	1.010	4	230	1.008	15.0	1.8
		Same case.....	.....	..	..	..	..	1.008	3	85	1.008		
5958	23	Chronic interstitial nephritis...	210–110	+	+	+	+	1.010	2	706	1.009	16.0	6.0
		Same case.....	.....	..	..	..	..	1.010	2	1,160	1.009		
3222	19	Acute nephritis.....	116– 60	—	—	+	+	1.014	6	890	1.011	23.7	3.6
		Same case.....	.....	..	..	..	..	1.012	7	780	1.011		
5037	20	Nephritis.....	192–102	+	—	+	+	1.016	9	710	1.016	26.6	3.3
5640	19	Nephritis.....	145– 85	—	—	+	+	1.013	4	567	1.010	12.0	
		Same case.....	.....	..	..	..	..	1.015	5	360	1.015		
4159	37	Syphilitic nephritis.....	120– 75	—	+	+	+	1.016	5	880	1.011	26.6	3.5
5584	50	Cardiorenal sclerosis.....	182–112	+	—	—	—	1.026	3	415	1.023	26.0	
		Same case.....	.....	..	..	..	..	1.019	4	510	1.019		
5794	49	Cardiorenal sclerosis.....	225–120	+	—	+	+	1.015	2	100	1.013	13.0	3.2
		Same case.....	.....	..	..	..	..	1.016	6	85	1.012		
4447	45	Cardiorenal sclerosis.....	160–110	—	—	+	+	1.018	10	2,840	1.008	22.0	7.3
3078	69	Arteriosclerosis.....	140– 90	+	—	+	—	1.020	3	400	1.017	12.9	5.6
4725	64	Arteriosclerosis.....	195–110	+	+	+	+	1.015	6	505	1.015	29.0	3.5
3653	51	Arteriosclerosis.....	184–140	+	+	+	+	1.017	8	450	1.017	15.0	7.0
4436	62	Arteriosclerosis.....	160– 92	+	—	—	+	10.20	8	335	1.020	26.0	3.6
4029	50	Arteriosclerosis.....	150– 98	+	+	+	+	1.027	22	215	1.027	24.0	5.2
4511	60	Arteriosclerosis.....	172	—	—	+	+	1.018	9	505	1.018	27.0	3.5
5055	28	Hysteria.....	122– 65	—	—	+	—	1.013	9	600	1.013	14.7	3.4

TABLE 2.—Cases Showing a Slight Abnormality in the Renal Dietary Test or Blood Analysis

Clinical Number	Age	Diagnosis	Blood Pressure	Heart	Edema	Albumin	Casts	Maximum Sp. Gr.	Variation Sp. Gr.	Night Urine		Blood	
										Volume, C.c.	Sp. Gr.	Urea N, Mg. per Cent.	Uric Acid, Mg. per Cent.
3199	55	Chronic interstitial nephritis..	200-100	+	—	+	—	1.022	2	240	1.020	17.9	3.5
		Same case.....	.....	..	..	..	..	1.024	4	260	1.023		
3301	21	Chronic interstitial nephritis...	148- 48	+	—	+	+	1.033	18	250	1.033	18.6	6.4
		Same case.....	.....	..	..	..	..	1.023	16	276	1.022	13.5	5.1
		Same case.....	.....	..	..	..	..	1.027	24	228	1.027		
5356	18	Chronic interstitial nephritis...	190-110	+	—	—	+	1.021	11	575	1.013	23.4	2.4
4224	44	Chronic interstitial nephritis...	140- 80	—	—	—	+	1.020	12	725	1.014	28.0	2.8
Ped.	10	Chronic interstitial nephritis...	108- 86	+	+	+	+	1.022	9	109	1.022		
4682	33	Chronic interstitial nephritis...	140- 80	+	—	+	+	1.025	16	197	1.025	22.4	1.0
3996	23	Chronic interstitial nephritis...	130- 64	—	—	—	—	1.022	15	365	1.022	18.0	4.0
3560	22	Chronic interstitial nephritis...	150- 90	—	+	+	+	1.020	15	370	1.014	10.0	3.2
		Same case.....	... ...	..	..	..	..	1.020	8	530	1.020	6.7	3.3
3856	29	Chronic interstitial nephritis...	140- 90	—	—	—	—	1.019	17	400	1.018	18.6	4.2
3451	56	Chronic interstitial nephritis...	194-126	—	—	+	—	1.020	13	1,000	1.007	14.4	1.5
3309	32	Chronic interstitial nephritis...	158- 90	—	—	+	+	1.030	7	380	1.026	19.0	4.0
3200	50	Chronic interstitial nephritis...	220-110	+	—	+	+	1.021	9	700	1.012	16.3	2.7
		Same case.....	.....	..	..	.	..	1.020	4	555	1.017		
4952	38	Chronic interstitial nephritis...	240-140	+	—	+	+	1.020	4	365	1.018	21.0	3.4
4951	40	Chronic interstitial nephritis...	172-105	+	—	—	—	1.013	10	885	1.013	16.5	1.6
5834	33	Chronic interstitial nephritis...	144- 88	+	—	+	—	1.023	13	280	1.021	16.1	3.7
		Same case.....	.....	..	..	..	..	1.027	4	275	1.026		
5084	44	Chronic interstitial nephritis...	135- 87	—	—	+	+	1.021	8	205	1.019	13.2	2.7
		Same case.....	.....	..	..	..	..	1.016	8	405	1.016		
5971	66	Chronic interstitial nephritis...	198-120	+	+	+	+	1.016	8	440	1.010	14.6	4.5
		Same case.....	.....	..	..	..	..	1.017	3	360	1.017		
4150	18	Chr. parenchymatous nephritis.	145-100	—	..	+	+	1.022	14	303	1.022	23.1	2.4
5050	24	Chr. parenchymatous nephritis	130- 78	+	+	+	+	1.025	14	455	1.012	19.0	2.7

3166	29	Acute parenchymatous nephritis	155- 90	−	+	..	..	1.016	11	170	1.015	13.7	2.5
		Same case	.....	..	..	..	..	1.018	4	190	1.018		
4215	22	Acute nephritis	122- 84	−	+	+	+	1.028	18	262	1.028	19.1	4.9
		Same case	.....	..	..	..	..	1.032	18	259	1.025		
Ped.	3	Acute nephritis	.....	−	+	+	+	1.024	11	91	1.022	22.4	3.9
5933	58	Chronic interstitial nephritis	127- 87	+	−	+	+	1.014	7	250	1.014	14.2	3.5
		Same case	.....	..	..	..	..	1.018	11	335	1.018		
3144	45	Cardiorenal sclerosis	135- 85	+	−	+	+	1.019	11	562	1.013	14.0	2.9
4129	55	Cardiorenal sclerosis	160- 90	+	−	−	+	1.024	9	225	1.024	15.4	4.7
4572	45	Cardiorenal sclerosis	186- 90	+	−	+	+	1.027	18	218	1.027	23.0	2.4
3113	61	Arteriosclerosis	159- 90	−	−	+	+	1.018	15	544	1.018	16.8	2.0
		Same case	.....	..	..	..	..	1.018	17	370	1.017		
3545	52	Arteriosclerosis	218-128	+	−	−	+	1.018	8	380	1.018	11.7	4.2
		Same case	.....	..	..	..	..	1.022	7	230	1.020	18.2	4.0
3017	50	Arteriosclerosis	248-170	+	−	+	+	1.030	10	200	1.030	16.8	3.0
4142	52	Arteriosclerosis	130- 60	+	−	+	+	1.031	20	230	1.028	16.0	5.0
4234	38	Arteriosclerosis	150- 80	..	−	+	+	1.027	9	220	1.027	12.0	3.8
4507	57	Arteriosclerosis	198- 98	+	−	−	+	1.020	14	250	1.020	23.0	2.0
4220	66	Arteriosclerosis	144- 80	+	−	−	−	1.022	15	320	1.022	26.0	3.2
3550	52	Arteriosclerosis	210-110	+	−	+	+	1.023	8	250	1.019	18.0	3.4
4070	55	Arteriosclerosis	200-120	+	−	+	+	1.021	8	325	1.020	18.6	3.2
4094	58	Arteriosclerosis	215-155	+	−	−	−	1.025	4	380	1.025	23.8	1.4
3120	59	Arteriosclerosis	240-100	+	−	+	+	1.018	6	387	1.018	11.4	3.5
3027	18	Renal tuberculosis	120	-	−	+	−	1.027	19	940	1.010	14.0	1.7
	28	Renal tuberculosis	135- 87	-	−	+	+	1.023	7	340	1.019	17.7	5.2
		Same case	.....	..	..	..	..	1.023	5	240	1.021		
4944	25	Hematuria	126- 55	−	−	+	−	1.020	11	345	1.020	30.8	3.1
5578	50	Cardiac decompensation	.....	+	+	+	+	1.023	8	280	1.025	16.2	
		Same case	.....	..	..	..	..	1.023	19	1,110	1.008		
4973	15	Endocarditis	115- 70	+	+	+	+	1.034	11	160	1.034	17.5	3.1
4171	23	Trichiniasis	110- 78	−	+	+	−	1.027	24	450	1.007	11.2	1.0
4985	24	Facial paralysis	180-110	−	−	+	+	1.020	15	265	1.020	26.8	3.2
5739	19	Peliosis rheumatica	126- 68	+	−	−	−	1.015	6	475	1.015	14.0	
		Same case	.....	..	..	..	..	1.024	12	515	1.023		
5866	47	Arthritis deformans	120- 72	−	−	−	−	1.024	12	330	1.012	12.3	5.1
		Same case	.....	..	..	..	..	1.026	11	155	1.026		
3299	27	Hysteria	128- 80	−	−	−	−	1.026	8	275	1.026	21.0	1.0
4680	19	Peripheral neuritis	110- 76	−	−	−	−	1.027	20	385	1.023	26.0	
Oph.	29	Iridocyclitis	128	−	−	−	−	1.026	6	260	1.021	15.1	3.8

TABLE 3.—Cases Showing No Abnormality in the Renal Dietary Test or Blood Analysis

Clinical Number	Age	Diagnosis	Blood Pressure	Heart	Edema	Albumin	Casts	Maximum Sp. Gr.	Variation Sp. Gr.	Night Urine		Blood	
										Volume, C.c.	Sp. Gr.	Urea N, Mg. per Cent.	Uric Acid, Mg. per Cent.
3908	27	Chronic interstitial nephritis...	100–95	—	—	—	+	1.022	14	270	1.018	18.0	1.7
3361	45	Chronic interstitial nephritis...	210–110	+	—	+	—	1.025	13	325	1.025	13.0	1.0
3089	27	Chronic interstitial nephritis...	122–78	—	—	+	+	1.028	16	260	1.028	15.0	2.5
3071	38	Chronic interstitial nephritis...	180–120	—	—	+	—	1.022	9	350	1.020	17.0	1.8
3087	37	Chronic interstitial nephritis...	130–85	—	—	+	—	1.019	17	325	1.019	16.0	1.8
5583	48	Chronic interstitial nephritis...	120–70	+	—	+	+	1.019	13	407	1.019	16.0	1.4
6006	32	Chronic interstitial nephritis...	140–90	+	—	+	+	1.027	10	170	1.027	14.2	1.8
		Same case.....	.....	..	..	..	..	1.033	10	200	1.033		
6016	45	Chronic interstitial nephritis...	104–78	—	—	—	+	1.032	10	300	1.033		
		Same case.....	.....	..	..	..	..	1.033	10	150	1.033	22.0	1.9
6077	43	Chronic interstitial nephritis...	198–110	+	+	+	+	1.024	12	345	1.024	11.6	1.9
6106	26	Chronic interstitial nephritis...	150–100	+	—	+	+	1.035	24	300	1.021	17.4	1.9
		Same case.....	.....	..	..	..	..	1.031	19	140	1.031		
6145	47	Chronic interstitial nephritis...	170–110	+	+	+	+	1.021	15	215	1.021	15.4	1.6
6091	51	Chronic interstitial nephritis...	140–78	—	—	+	—	1.025	20	190	1.021	16.4	2.1
		Same case.....	.....	..	.	..	..	1.024	15	205	1.024		
3339	25	Acute nephritis.....	140–60	+	+	+	+	1.019	12	325	1.018	14.0	1.2
5736	18	Albuminuria.....	120–75	—	—	+	+	1.025	16	220	1.016	18.0	
5050	24	Nephrosis.....	120–88	—	+	+	+	1.029	9	220	1.020	7.7	2.6
		Same case.....	.....	..	..	..	..	1.029	9	205	1.021		
4209	49	Arteriosclerosis.....	210–110	.	—	—	+	1.027	20	345	1.018	21.0	1.0
3035	57	Arteriosclerosis	175–95	—	—	—	—	1.030	20	220	1.020	8.0	2.5

4049	32	Pregnancy	128- 68	—	—	+	+	1.024	10	330	1.024	25.0	1.0
Gyn.	23	Pregnancy	110- 60	—	—	—	—	1.020	12	300	1.020	18.0	1.0
Gyn.	30	Pregnancy	120- 60	—	—	—	+	1.023	17	170	1.023	16.0	1.5
5995	14	Congenital syphilis	120- 68	—	—	—	—	1.021	13	190	1.021		
		Same case	.....	..	..	..	..	1.026	20	250	1.026		
6021	45	Cerebrospinal syphilis	100- 50	—	—	—	—	1.020	14	160	1.020		
		Same case	.....	..	..	..	..	1.025	20	290	1.025		
6048	28	Neurasthenia	130- 60	—	—	+	—	1.024	18	130	1.024	11.4	1.8
		Same case	.....	..	..	..	..	1.032	10	140	1.032		
5960	24	Neurasthenia	135- 68	—	—	+	+	1.028	20	202	1.028	11.4	1.4
		Same case	.....	..	..	..	..	1.035	31	220	1.035		
5495	18	Neurasthenia	118- 50	—	—	—	—	1.030	15	232	1.025	16.0	1.5
6042	30	Neurasthenia	115- 58	—	—	+	—	1.025	18	160	1.025		
		Same case	.....	..	..	..	..	1.026	22	195	1.026		
4960	21	Primary optic atrophy	120- 80	—	—	—	—	1.029	18	300	1.025	16.0	2.0
5937	15	Chorea	.....	—	—	—	—	1.031	16	155	1.031		
		Same case	.....	..	..	..	..	1.029	23	210	1.029		
5789	42	Morphinism	135- 90	—	—	+	+	1.021	17	245	1.021	16.0	1.5
		Same case	.....	..	..	..	..	1.029	15	232	1.022		
5808	52	Acromegaly	126- 70	—	—	—	—	1.029	12	348	1.029	18.0	1.3
		Same case	.....	..	..	..	..	1.035	13	222	1.030		
6036	16	Polyglandular insufficiency	110- 65	—	—	—	—	1.023	15	312	1.023		
		Same case	.....	..	..	..	..	1.023	17	280	1.023		
Surg.	15	Hyperthyroidism	135	—	—	—	—	1.036	14	98	1.036	13.2	1.4
		Same case	.....	..	..	..	..	1.029	19	120	1.029		
6072	26	Gonorrheal rheumatism	112- 70	—	—	—	—	1.028	11	280	1.028	15.4	1.9
6151	31	Hysteria	128- 72	—	—	—	—	1.024	10	155	1.024		
		Same case	.....	..	..	..	..	1.028	19	180	1.028		
6050	18	Bronchopneumonia	.....	—	—	—	—	1.020	12	400	1.020		
		Same case	.....	..	..	..	..	1.025	19	350	1.019		

DISCUSSION

Depending in a general way on the degree of abnormality, the cases have been tabulated in three groups. The cases showing marked abnormality have been omitted. In addition to the laboratory findings, the clinical number, age, diagnosis, systolic and diastolic blood pressures, presence of cardiac enlargement, edema, albumin and casts have been considered. The following norms have been adopted for the dietary tests and blood analyses: Maximum specific gravity, eighteen or higher; variation in specific gravity nine or more; volume of the night urine 400 c.c. or less; specific gravity of the night urine eighteen or more; urea nitrogen concentration of the blood 0.020 grams per cent. or less, and the uric acid concentration of the blood 0.0025 grams per cent. or less.

Tables 1 and 2 summarize the data of 100 cases showing moderate and slight abnormality, respectively. All showed renal involvement from the clinical point of view. *Sixty-six per cent. had an abnormality in the dietary test, while 74 per cent. showed an increased concentration of uric acid in the blood.* Myers and collaborators[5] have pointed out that in nephritis the uric acid content of the blood is increased long before urea. Mosenthal and Lewis[6] compared the delicacy of the various tests for renal function, but omitted consideration of the blood uric acid. They concluded that the dietary test was the most delicate.

It follows from the above that the uric acid concentration of the blood is a delicate, if not the most delicate, index of renal function at our disposal. The individual abnormalities in our series were as follows: Twenty-six as regards maximal specific gravity, forty-nine as regards variability of specific gravity, forty as regards volume or concentration of the night urine and thirty-five as regards urea nitrogen content of the blood. An abnormal dietary test with normal blood findings was found in 8 per cent. of the cases. An abnormally high urea with a normal uric acid concentration was encountered in only six instances. The figures in Tables 1 and 2, but particularly those in Table 3 indicate that 400 c.c. is the upper normal limit for the volume of the night urine, provided the patients are kept in bed during the test period. At any rate we have never found more in an individual in whom there was no reason to suspect renal involvement.

If each test is considered as a whole, the figures of Table 4 indicate that the results are similar with either the bland or the relatively

5. Myers, V. C., and Fine, M. S.: J. Biol. Chem. **20**:391, 1915. Myers, V. C.; Fine, M. S., and Lough, W. G.: Arch. Int. Med. **17**:570, 1916. Chace, A. F., and Myers, V. C.: J. A. M A **67**:929, 1916.

6. Mosenthal, H. O., and Lewis, D. S.: J. A. M. A. **67**:933, 1916.

high protein and salt diets. Owing to the small quantity of solids which it contains, the bland diet tends to lower the specific gravity of the night urine. As one would expect in cases with fixation of specific gravity the volume of the night urine is greater on the regular than on the bland diet. On the whole, it appears that both tests may be used interchangeably. The advantages of the bland diet are that it is easily prepared, and that it may be used where a high protein diet is undesirable or where digestive disturbances are present.

TABLE 4.—COMPARISON OF THE DATA OF BOTH DIETARY TESTS, BLAND AND REGULAR

Maximum Sp. Gr.		Variation Sp. Gr.		Total Volume, C.c.		Night Urine			
						Volume, C.c.		Sp. Gr.	
Bland	Regular	Bland	Regular	Bland	Regular	Bland	Regular	Bland	Regular
1.010	1.010	2	2	1,764	2,783	760	1,160	1.009	1.009
1.021	1.026	10	17	1,070	1,066	290	310	1.021	1.025
1.022	1.020	16	16	1,128	1,754	395	304	1.015	1.020
1.020	1.020	16	14	1,305	1,185	290	350	1.020	1.020
1.026	1.019	3	4	853	1,194	415	510	1.023	1.019
1.015	10.13	5	4	1,163	1,340	360	567	1.015	1.010
1.017	1.021	6	3	1,508	1,127	615	500	1.017	1.021
1.029	1.035	12	13	744	492	348	222	1.020	1.030
1.015	1.016	2	8	593	944	100	85	1.013	1.012
1.022	1.036	22	31	1,013	600	257	165	1.009	1.029
1.015	1.024	6	12	1,694	1,436	457	515	1.015	1.023
1.015	1.020	9	4	1,807	1,177	567	515	1.015	1.019
1.021	1.029	17	15	1,287	561	245	232	1.021	1.022
1.010	1.008	4	3	762	671	230	85	1.008	1.008
1.022	1.019	16	10	1,016	1,092	380	310	1.016	1.017
1.023	1.027	13	3	808	676	280	275	1.021	1.026
1.025	1.030	16	10	1,213	641	320	232	1.016	1.030
1.009	1.010	0	1	1,506	1,705	845	935	1.009	1.009
1.025	1.024	17	7	1,809	1,343	370	490	1.025	1.024
1.024	1.026	18	11	966	590	330	155	1.012	1.026
1.033	1.033	9	9	678	833	300	150	1.033	1.033
1.021	1.016	8	7	823	1,600	205	405	1.019	1.016
1.029	1.022	9	12	370	757	220	510	1.020	1.010
1.016	1.017	8	3	1,300	670	440	360	1.010	1.017
1.028	1.035	20	31	1,157	1,570	202	220	1.028	1.035
1.014	1.018	7	12	1,595	1,652	250	335	1.014	10.18
1.028	1.027	24	17	979	963	305	312	1.016	1.026
1.024	1.032	18	10	1,405	920	120	140	1.024	1.032
1.027	1.033	10	12	447	507	170	200	1.027	1.033
1.021	1.026	13	20	1,638	2,315	190	250	1.021	1.026
1.031	1.029	16	23	674	1,377	155	210	1.031	1.029
1.025	1.026	18	22	1,315	1,750	160	195	1.025	1.026
1.020	1.025	14	20	1,460	2,680	160	290	1.020	1.025
1.028	1.026	11	16	700	1,120	280	280	1.028	1.026
1.035	1.031	24	19	953	836	300	140	1.021	1.031
1.023	1.023	15	17	1,467	2,180	312	280	1.023	1.023
1.020	1.025	13	19	1,700	1,575	400	350	1.020	1.019
1.036	1.029	14	19	224	725	98	120	1.036	1.029
1.022	1.034	17	24	1,690	1,262	700	950	1.014	1.010
1.024	1.028	10	19	590	657	155	180	1.024	1.028

CONCLUSIONS

In conclusion, we wish to emphasize the desirability of keeping the patients in bed during the test period. Even then the results may be unreliable in the presence of edema, cardiac decompensation or when the urine is scanty or highly concentrated as in midsummer. Needless to say all forms of treatment must be interdicted during the test period.

ON THE CLINICAL EVIDENCE OF INVOLVEMENT OF THE SUPRARENAL GLANDS IN INFLUENZA AND INFLUENZAL PNEUMONIA *

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During the recent epidemic of influenza and influenzal pneumonia, we were impressed with the marked degree of asthenia present in all cases. No matter how mild the attack, asthenia was almost invariably one of the most, if not the most, prominent symptom. It was usually out of all proportion to the other symptoms and persisted not only during the attack but far into convalescence. When we review the summaries of chief complaints recorded in the literature, we find that this was the general observation. Certain symptoms were more common in some localities than in others, but asthenia was the symptom common to the disease in all localities.

In our series of cases[1] we were unable to satisfy ourselves with the prevailing belief that the prostration was due to cardiovascular disease. Our attention was called to the possible existence of disturbed function of the suprarenal glands early in the epidemic, whereupon we instituted epinephrin treatment in a series of cases.

The most common and the most marked symptom of suprarenal insufficiency is asthenia (prostration). Low blood pressure, another cardinal symptom of suprarenal insufficiency, has been commonly observed by clinicians as characteristic of influenza and influenzal pneumonia. We became interested in determining, on purely clinical grounds, if possible, whether a hypoadremia or a disturbance of the chromaffin system could be shown to be at the bottom of the symptom group so much in the foreground in this disease.

The French school, among whom should be mentioned Josue,[2] Netter,[3] Sergent,[4] Renon[5] and Florand,[6] has emphasized its belief that

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* Read at the Meeting of the American Society for Clinical Investigation, Atlantic City, June 14, 1919.

1. Cowie, D. M., and Beaven, P. W., Jr.: J. Michigan M. S. **18**:42 (Feb.) 1919.
2. Josué: Bull. et mem. Soc. med. d. hôp. de Par. 904 (Oct. 11) 1918.
3. Netter, A.: Ibid. p. 903.
4. Sergent, E.: Ibid. p. 905.
5. Rénon, L.: Ibid. p. 905, quoted by Sergent.
6. Florand, A.: Ibid. p. 905, quoted by Sergent.

suprarenal pathology is present in influenza and is responsible for the symptom of asthenia. In this country Kelman and Calhoun[7] found evidence of suprarenal dysfunction in a series of over twenty necropsies.

Demonstration of Suprarenal Insufficiency in Many of the Acute Infections.—In 1900, Evans[8] reported a case of typhoid fever in which during convalescence symptoms of suprarenal insufficiency began to develop—marked asthenia, low blood pressure, bronze skin and diarrhea. Evans asks whether suprarenal insufficiency is a complication of a primary condition, typhoid in this instance. Lavenson[9] has shown that from an adjacent suppurative process in the lungs thrombosis of the suprarenal veins may occur and bring about a necrosis of the suprarenals. Dock[10] remarks that lung conditions, such as pneumonia, favor inflammation and softening of the suprarenals.

Probably the most striking illustrations of pneumonias so complicated are to be found in the cases reported by Murray,[11] Greenhow[12] and Sicard.[13] Murray's case was a severe pneumonia which presented, in addition to the pneumonic symptoms, remarkable prostration and a general duskiness of the skin. The mucous membranes were not involved. This patient died, apparently from exhaustion. Necropsy showed an extravasation of blood into both suprarenal capsules. The center of the right capsule was plugged with a firm black clot. Greenhow's case was a pneumonia, the chief symptom of which was weakness, which continued throughout the disease until death. In this case the right suprarenal was found to be enlarged, firm and fibrous; the left suprarenal was converted into a sac filled with a coagulum. Sicard's case was a bacillus Friedländer's pneumonia, the chief symptom of which was also asthenia. The asthenia was so marked that the patient presented signs difficult to differentiate from those of bulbospinal myasthenia. Necropsy showed hemorrhage into the center of both suprarenals.

The opinion is fixed so firmly that the suprarenals are involved in many of the acute infections that the French school, fathered by Sergent,[14] assumes its presence, and claims one is justified in making a diagnosis of suprarenal insufficiency whenever the characteristic

7. Kelman, S., and Calhoun, H.: Personal communication.
8. Evans, H. W.: Lancet **1**:1655 (June 9) 1900.
9. Lavenson, R. S.: Arch. Int. Med. **2**:68 (Oct.) 1908.
10. Dock, G.: Osler's Syst. Med. **4**:783.
11. Murray, J.: Trans. Path. Soc., Lond. **21**:395, 1870.
12. Greenhow, E. H.: Tr. Path. Soc. Lond. **28**:231, 1877.
13. Sicard, M., Soc. med. d. hôp. d. Par., p. 848, 1904.
14. Sergent: Arch. gen. de med. **193**:17, 1904.

symptoms can be demonstrated. Sergent[15] believes that this complication follows certain infections as regularly as nephritis follows scarlet fever, and in precisely the same manner. Chief among the supporters of this idea is Bossuet.[16] Indeed, few of the French clinicians dissent from Sergent's view.

Pathologic Evidence That the Suprarenals Are Affected in Influenzal Pneumonia.—While this is purely a clinical and not a pathologic study, it is, nevertheless, of paramount interest to know whether necropsies performed in cases of influenzal pneumoia throw any light on the question. The findings of Kelman and Calhoun,[7] to which we have already referred, are significant. Through the courtesy of the department of pathology, we have reports of the suprarenal findings in eleven cases of influenzal pneumonia. It is unfortunate that we cannot present more cases. These were all necropsies permitted by the military authorities on over seventy patients belonging to the S. A. T. C. who died of the disease.

In these necropsies, six cases showed hypoplasia, and one case a moderate atrophy, but in no cases did hemorrhage into or necrosis of the suprarenals occur. The hypoplasia, however, was associated with a "status lymphaticus" in all but one case.

We must admit that from the records of the pathologic department we have not a clear case of suprarenal disease, but surely one which raises the question: Does hypoplasia of the gland signify its hypofunction? In this particular group of cases, we think no other question can arise. It may not be out of place, at this point, to call attention to the fact, so frequently demonstrated, that an organ may fail to functionate almost, if not completely, so far as certain of its secretions are concerned and yet give no evidence of anatomic change (the gastric mucosa in pernicious anemia and achylia gastrica).

Symptoms of Suprarenal Insufficiency.—The chief symptoms of suprarenal insufficiency are asthenia, prostration and lowered blood pressure. These are alike common to acute or chronic suprarenal insufficiency. In our series of influenza and influenzal pneumonia cases, these findings were invariably present, but there were other symptoms common to the disease which are characteristic of acute suprarenal insufficiency not of influenzal origin, such as nausea, vomiting, abdominal pain (epigastric and appendiceal), pains in the back and even tenderness on pressure over the back muscles, and in a few cases diarrhea. Lavenson has attempted a grouping of various symptoms presented by the cases of known suprarenal insufficiency which have

15. Sergent, E.: J. de med., 753 (Oct. 10) 1917.
16. Bossuet, G.: Gaz. hebd. d. sc. méd. de Bordeaux, **25**:524, 1904, quoted by Lavenson (9).

been recorded, and he describes (1) what may be called the abdominal type in which sudden death was preceded by marked abdominal symptoms; (2) the asthenic type; (3) the nervous type characterized by convulsions, and (4) cases of sudden death in which at necropsy no pathology except that present in the suprarenals could be found. In influenza and influenzal pneumonia it is not difficult to differentiate cases suitable to the first three groupings. We will discuss other, possibly more definite, signs of suprarenal insufficiency in the following paragraphs.

Tests for Suprarenal Insufficiency.—Blood Pressure: We took pressures on a group of unselected cases with no regard to the stage of the disease. Five were cases complicated with pneumonia and twenty were uncomplicated influenzas. The average systolic pressure of the pneumonias was 99. The average systolic pressure of the influenzas was 115. This is a lowered pressure when one takes into consideration the fact that the patients ranged in age from 20 to 40. In one case of influenza the blood pressure was 105. The patient, a medical student, stated that he had had his blood pressure taken previous to the disease and it had registered 130 systolic. Keeton and Cushman report that in a series of fifty-seven observations 42 per cent. of the patients had systolic pressures of 110 or below. Josue[2] states that in almost every case of influenza that came under his observation the patient had a low blood pressure even if pneumonia did not complicate the case.

Low blood pressure is the rule in suprarenal insufficiency whether it is caused by tuberculosis, syphilis, cirrhosis or hemorrhage into the suprarenals, and whether it is acute or chronic. Dock[10] records four cases of Addison's disease in which the pressures were 110, 108, 85 and 83. In two other cases taken from his records in this hospital,[17] we find the systolic pressure in one case varying between 85 and 110, in the other between 84 and 107. In the case we record in Table 1, the systolic pressure varied between 84 and 100. Higher blood pressures have been recorded in Addison's disease. Janeway has reported a case in which the systolic pressure was 140. This, however, is a very rare finding. Gruenbaum,[18] in a synopsis of his cases of Addison's disease, concludes that the systolic pressure averages about 100. Schaffner and Howard[19] report one of the few cases of syphilitic involvement of the suprarenal gland. In this case the systolic pressure was 98. In Sergent's[14] case of fibrosis of the suprarenals there was a marked arterial hypotension. In Sicard's[13] case of acute suprarenal

17. Numbers 08-623 and 05-38.
18. Gruenbaum, O.: Practitioner, Lond. **79**:218 (Aug.) 1907.
19. Schaffner, P. M., and Howard, T.: New York M. J. 1026, (May 27) 1916.

insufficiency, where necropsy revealed hemorrhage into the gland, the systolic pressure was 78 (or 7.8 Potain's sphygmomanometer). It is not unreasonable to conclude that the blood pressure observed in influenza and especially in the complicating pneumonia, corresponds to what we should expect to find.

We must consider the fact that low blood pressures are commonly found in certain other diseases not of influenzal origin, for example, diphtheria[20] and croupous pneumonia. These diseases present this finding when the myocardium is weakned, and at such a time, unquestionably, this defect plays a rôle in bringing about the reduced pressure. It is known that diphtheria toxin in the circulation calls forth all the available epinephrin to combine with it and render it harmless.[21] That epinephrin antagonizes diphtheria toxin has been shown by injecting it at the time of, or shortly after, injecting a fatal dose of diphtheria toxin, in which case the animal survives.[21]

One can conceive of the demand for epinephrin by the toxin being so great as to exhaust the suprarenals and other chromaffin tissues, and thus cut off one of the potent factors in sustaining normal blood pressure. We have previously cited instances of pneumonia in which the suprarenals were involved. We are not sure that this is not a common occurrence and that it may be responsible for the lowered pressure in this disease. It is not at all improbable that the pathologist's zeal to seek for signs of dysfunction in this organ has been no less marked than that of the clinician's to interpret the significance of what have been determined to be quite well-marked manifestations of adrenal insufficiency.

In our series of cases referred to before,[1] we were unable to demonstrate evidence of significant weakened heart action. To us it seems credible to regard the lowered blood pressure in influenza and influenzal pneumonia as due to causes other than those of myocardial origin. It may be endocrinal.

Rise of Systolic Pressure After Prolonged Administration of Epinephrin.—After giving suprarenal extract in 3-grain doses, three times daily, in cases of suprarenal deficiency, Gruenbaum[18] reports a rise of 10 mm. Hg at the end of the third day, which did not occur in the control cases. Of five influenzal patients, whom we selected to test out this point, one was in the acute stage of the disease, and subsequent observation showed that he was developing pneumonia at the time of the test. This patient had a systolic pressure of 119 before the epinephrin was given. He was given 10 minims of epinephrin[22]

20. A case in our clinic showed a systolic pressure of 84.
21. Marie, A.: Ann. de l'Inst. Pasteur, March, 1918.
22. Fresh adrenalin (Parke, Davis & Co.), 1:1,000 solution, was used in all experiments.

intramuscularly, four times daily, for three days. At the end of this time his pressure was taken with the precaution that five hours had elapsed since the last injection. It was found to be 131. In the other four cases, treated in the same way, with the patients convalescent at the time of the test, no effect on the blood pressure was observed. In the control cases (patients in hospital for other reasons) no rise in pressure was noted. If this test is as valuable as Gruenbaum regards it, we may assume a suprarenal insufficiency in the first case cited, an acute case.

Maintenance of Pressure with Epinephrin.—Two years ago Beaven studied a case of Addison's disease in the medical clinic (No. 17-546) in which the diagnosis was confirmed by necropsy. He made the following observations: If 1 c.c. of epinephrin was injected intramuscularly, after the initial rise, the systolic pressure would remain elevated longer than it would in a normal individual. The result of this case together with that of a series of influenza and normal cases is given in Table 1.

TABLE 1.—The Effect of Epinephrin on the Blood Pressure Curve

Case Number	Name	Diagnosis	Control Pressure	Systolic Blood Pressure after Subcutaneous Injection of 1 Mg. Epinephrin					
				1 Hour	2 Hours	3 Hours	4 Hours	5 Hours	7 Hours
1	.....	Addison's	84	112	...	96			
2	C. F.	Pneumonia	103	118	120	113	...	108	103
3	J. N.	Pneumonia	90	142	99	99	...	91	
4	W. T.	Influenza	128	140	148	135	...	128	
5	E. M.	Influenza	106	...	120	...	110	105	
6	C. S.	Influenza	105	...	128	...	118	104	
7	A. L.	Influenza	106	...	126	115	106	105	
8	A. R.	Mumps	130	135	128	125	...	132	
9	P. B.	Normal	130	126	118	115	...	120	
10	C. H.	Normal	112	118	106	108	...	110	

This table shows that the cases of influenza and influenzal pneumonia simulate the result obtained in Addison's disease. The normal cases reached their height a few minutes after the injection, and at the end of an hour the pressure had returned, practically, to normal. At the end of two hours, the pressure was normal in both cases. The mumps case also follows the normal curve. The analogy presented by this investigation may be significant.

The Leukocytic Picture.—We have shown, and so have others,[1, 23] that a low leukocyte count and a tendency to a leukopenia is the rule in influenza and influenzal pneumonia of the adult type. When we take from a series of ninety cases all those patients who lived, on the one hand, and all those who died, on the other, we obtain the following

23. Keeton, R. W., and Cushman, A. B.: J. A. M. A. **71**:1964, 1918.

averages in the leukocyte counts. Those that lived had a white count of 8,300 made up of polymorphonuclears, 75 per cent. and lymphocytes, 25 per cent. Those who died had a white count of 6,500, of which 61 per cent. were polymorphonuclears and 39 per cent. were lymphocytes. We observe that there is practically a normal leukocyte count, and that the differential count is not changed markedly. This is the same blood picture one finds in Addison's disease.[10] and it is interesting to note that the same low count and tendency to a leukopenia is present in typhoid fever, a disease which is also characterized by low blood pressure.[24]

Tests for Endocrinal Dysfunction Applied to Influenza and Influenzal Pneumonia.—A. Blood Sugar: One of the frequent findings in disturbances of endocrinal origin is a hypoglycemia.[25] We have made blood sugar determinations in a series of thirteen influenza cases and eight influenzal pneumonia cases with this point in view. None of the cases recorded had received any epinephrin during the course of their illness. The estimations were made at various stages of the disease, and the blood samples were taken at least three hours after the ingestion of food. The determinations were made by the Lewis and Benedict method, and are recorded in Table 2. It will be seen that the blood sugar was always within normal limits. There does not seem to be any relation between the period of the disease, the amount of prostration and the glycemia. We call attention to this latter point in particular, because McCrudden and Sargent[26] explain the myasthenia of progressive muscular dystrophy on the basis of hypoglycemia. On the other hand, one cannot assume that a hypoglycemia is pathognomonic of endocrinal disturbance, since it is not always found, and since in certain endocrinal diseases a hyperglycemia is frequently found (exophthalmic goiter).

B. Blood Sugar Changes Following the Intramuscular Injection of 1 mg. of Epinephrin: The occurrence of a temporary rise in the normal blood sugar curve after the injection of epinephrin is well known. Not finding a hypoglycemia, we attempted to demonstrate a difference in the excretion curve after an artificial hyperglycemia induced by the epinephrin injection. Hamman and Hirschman[27] have shown that after the injection of one milligram of epinephrin in a diabetic (Cases 12 and 24) in place of the normal "prompt rise in the blood sugar

24. Carter, H. S.; Orr, and Norris, G. W.: Quoted by Morris and Edmunds, Med. News, Jan. 14, 1905.

25. Janney, N. W.; Goodhart, S. P., and Isaacson, V. I.: Arch. Int. Med. **21:** 188 (Feb.) 1918.

26. McCrudden, R. H., and Sargent, C. S.: Arch. Int. Med. **17:**471 (April) 1916.

27. Hamman, L., and Hirschman, I. I.: Arch. Int. Med. **20:**762 (Dec.) 1917.

which reached its maximum in a half to one hour, and then rapidly subsided, the whole reaction being over in two hours," there is a prolonged blood sugar curve characterized by a slow rise which may or may not be high, but is well sustained, and may not return to normal until beyond two and a half hours after the injection. We have applied this test to a series of influenza and influenzal pneumonia and control

TABLE 2.—BLOOD SUGAR DETERMINATIONS IN INFLUENZA AND INFLUENZAL PNEUMONIA

Case Number	Name	Diagnosis	Day of Disease	Degree of Prostration	Blood Sugar Reading
1	M. L.	Influenza	1	Acute	0.103
2	R. McC.	Influenza	2	Moderate	0.116
3	W. R.	Influenza	2	Acute	0.097
4	T. J.	Influenza	2	Moderate	0.104
5	D. S.	Influenza	2	Moderate	0.088
6	M. L.	Influenza	3	Mild	0.081
7	M. L.	Influenza	3	Mild	0.122
8	C. S.	Influenza	3	Acute	0.097
9	E. M.	Influenza	4	Acute	0.105
10	M. S.	Influenza	5	Mild	0.106
11	A. S.	Influenza	5	Mild	0.118
12	W. McK.	Influenza	7	Mild	0.142
13	E. M.	Influenza	10	Mild	0.104
14	L. T.	Pneumonia	1	Acute	0.132
15	P. M.	Pneumonia	2	Acute	0.120
16	C. F.	Pneumonia	3	Moderate	0.103
17	F. R.	Pneumonia	3	Acute	0.096
18	M. L.	Pneumonia	5	Acute	0.134
19	M. R.	Pneumonia	8	Acute	0.104
20	F. M.	Pneumonia	15	Acute	0.166
21	F. B.	Pneumonia	24	Moderate	0.107

TABLE 3.—THE EFFECT OF INJECTION OF 1 MG. EPINEPHRIN ON THE BLOOD SUGAR CURVE

Case Number	Name	Diagnosis	Stage of Disease	Control Blood Sugar	Blood Sugar after Subcutaneous Injection of 1 Mg. Epinephrin						
					1 Hr.	2 Hrs.	3 Hrs.	4 Hrs.	5 Hrs.	6 Hrs.	7 Hrs.
1	P. M.	Pneumonia	Acute	0.120	0.166	0.206	.....	.....	0.166	.....	0.136
2	C. F.	Pneumonia	Acute	0.103	0.130	0.141	.....	.....	0.118	.....	0.096
3	M.	Pneumonia	Acute	0.116	.....	0.200	0.142	0.153	0.156	0.142	
4	F. R.	Pneumonia	Moderate	0.096	0.134	0.108	0.102	.....	0.086	.....	0.097
5	E. M.	Influenza	Acute	0.105	.....	0.223	.....	0.133	0.100		
6	C. S.	Influenza	Acute	0.097	.....	0.137	.....	0.109	0.096		
7	M. L.	Influenza	Moderate	0.081	0.096	0.090	.....	.....	0.081	.....	0.084
8	T. J.	Influenza	Moderate	0.104	0.157	0.107	0.092	.....	0.098	.....	0.097
9	P. B.	Normal	.....	0.086	0.129	0.161	0.081	.....	0.079		
10	C. H.	Normal	.....	0.087	0.206	0.169	0.082	.....	0.078		
11	A. R.	Mumps	Acute	0.104	0.157	0.119	0.092	.....	0.096	.....	0.097

cases. We followed the blood sugar curve over a long period, often to the seventh hour without food ingestion during the period of observation. Our results are recorded in Table 3.

Cases 1, 2 and 3 show a distinct delay in the return of the blood sugar to normal. In Case 1 it had not returned to normal seven hours after the injection. In Case 2 it had not reached normal at the fifth hour, and in Case 3 it is not back to normal at the sixth hour. It may

be significant that Case 4 is practically back to normal at the third hour. Undoubtedly, had an observation been made, it would have been back to normal at the fourth hour. This was a case of pneumonia, but the patient was not acutely prostrated as were the other three. Cases 5 and 6, uncomplicated influenzas, show some delay, but it is not as marked as is that of the pneumonias, whilst Cases 7 and 8, influenzas of only moderate degree, in which the prostration was only slight, show blood sugar curves closely simulating those obtained in normal cases.

We believe these sustained blood sugar curves support the idea that endocrinal dysfunction is a factor in influenza and influenzal pneumonia, and that the degree of endocrinal involvement is proportional to the prostration. The long sustained blood sugar curves obtained by Hamman and Hirschman were observed only in endocranial disturbances, hyperthyroidism and diabetes.

TABLE 4.—The Effect of Glucose Ingestion on the Blood Sugar Curve

Case No.	Name	Diagnosis	Stage of Disease	Weight of Patient	Grams of Glucose Given	Control Blood Sugar	Blood Sugar after Ingestion of Glucose				
							1 Hr.	2 Hrs.	3 Hrs.	4 Hrs.	5 Hrs.
1	M. L.	Pneumonia	Acute	137	125	0.143	0.248	.....	0.179	.....	0.128
2	F. B.	Pneumonia	Convl.	80	75	0.107	0.152	.....	0.107	.....	0.107
3	W. R.	Influenza	Acute	162	150	0.097	0.246	.....	0.118	.....	0.104
4	M. S.	Influenza	Convl.	110	100	0.106	0.218	.....	0.127	.....	0.099
5	R. M.	Influenza	Convl.	155	125	0.116	.....	0.150	0.132	0.121	0.119
6	E. M.	Influenza	Convl.	112	100	0.104	.....	0.225	0.162	0.121	0.107
7	P. B.	Normal	.....	165	150	0.114	0.139	0.110	0.110		
8	C. H.	Normal	.....	137	125	0.093	0.110	0.098	0.096		

C. Blood Sugar Curve After the Ingestion of Glucose: Janney and Isaacson[23] call attention to the diagnostic value of the blood sugar curve following the ingestion of glucose in diseases of endocranial origin. They took the blood from a fasting patient for a control, and gave 1.75 gm. of glucose per kilogram of body weight. The blood was then analyzed for sugar at stated intervals. In a series of normal persons, they found that the glucose content of the blood returned to normal in two hours. In a patient with an endocrinal disturbance, the curve did not return to normal until the end of the third and sometimes of the fourth hour. They concluded that this delayed blood sugar excretion curve is significant of an endocrinal dysfunction of some character, though not indicative of any particular gland. We have applied this test in six influenza cases and two control cases, with results as shown in Table 4. The weight of the person and the amount of glucose ingested are indicated. We were not able to follow the exact directions given by Janney and Isaacson, because only reported weights of the patients could be obtained.

It will be seen from this series of observations that the normal blood sugar curve appears in only one of the six cases (Case 2), and that prolonged curves are present in the other five. Fourth hour observations were made in only two cases (Cases 5 and 6). In neither of these had the curve returned to normal. Normal blood sugar values were obtained in all cases at the fifth hour. Case 2, which presents a normal curve, was a patient convalescing from pneumonia. His temperature, pulse and respiration had been normal for three weeks. He had a bad cough and a few moist râles. Aside from this he was well and was in no way prostrated. We would expect this patient to show a normal blood sugar curve. This fact seems to show that the endocrinal dysfunction returns to normal completely during convalescence or when the asthenia disappears. It is important to state that this patient had a severe pneumonia and at that time was prostrated very markedly.

The variations from normal which we have observed in the blood sugar curve after the ingestion of glucose coincide with the results of Janney and Isaacson, and lend further support to the idea that influenza affects the internal secretory system.

Therapeutics of Epinephrin in Influenza. — The French school, notably Sergent, Josue, Netter and Renon, advocate the use of epinephrin in influenza by the subcutaneous and intramuscular routes, the latter having the preference because they found that the subcutaneous method depressed the patient. We used the intramuscular method entirely. Some patients received 10 minims every four hours, four times daily; other patients received 15 minims every four hours, four times daily. These patients were in the hospital during the early part of the epidemic. Almost invariably the patient reacted with palpitation, complained of nervousness, slight headache and increased lassitude, and, occasionally, marked twitching occurred. The temperature was raised slightly and the pulse and respiration generally showed a marked increase. In one case, in which the asthenia was marked, the blood pressure was definitely raised after prolonged administration of epinephrin. We came to the conclusion that epinephrin so administered at least was of little, if any, benefit, and discontinued its further use. Possibly the proper method of administering epinephrin has not yet been found.

CONCLUSIONS

1. Necropsy reports reveal hypoplasia of the suprarenals and evidence of suprarenal dysfunction.

2. The occurrence of suprarenal dysfunction in influenza and influenzal pneumonia may be regarded as indicated by the cardinal symp-

toms, the characteristic rise in blood pressure following the prolonged administration of epinephrin, and the prolonged blood pressure curve following the administration of epinephrin.

3. That an endocrinal disturbance is present in influenza and influenzal pneumonia is further suggested by prolonged blood sugar curve after injection of epinephrin; prolonged blood sugar curve after ingestion of glucose.

4. Hypoglycemia is not present in influenza and influenzal pneumonia as has been found to be the case in some diseases of endocranial origin.

5. If epinephrin is of any use in the treatment of the symptoms of suprarenal dysfunction, the proper method of administering the epinephrin seems not yet to have been found.

AUSCULTATORY PHENOMENA OF THE HEART IN NORMAL MEN AND IN SOLDIERS WITH IRRITABLE HEART

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In the examination of men in the army for cardiovascular diseases, one is continually impressed with the frequent occurrence of certain adventitious sounds and murmurs of the heart in men of apparently robust physique. The problem of determining whether certain sounds or murmurs other than the conventional "lub-dupp" of the heart-sounds should be considered significant of heart disease or as merely accidental phenomena belonging to normal hearts is often perplexing. It is a much more simple task for most of us to classify properly a mixed group of organic cardiac lesions, probably because physical diagnosis is taught in medical schools largely from the study of pathologic conditions, and also because it is seldom possible to study normal hearts in large enough numbers to allow us to clarify our ideas as to which deviations from the usual should be considered normal and which pathological.

It is often advised that the diagnosis of organic heart disease be made only in the presence of cardiac hypertrophy, but we are often forced to the conclusion that such a rule does not hold good. For example, the diagnosis of aortic insufficiency is made for us when we hear a murmur of a certain type in diastole; yet one sees many soldiers with aortic insufficiency who present no demonstrable hypertrophy of the heart nor, indeed, any other secondary sign of the lesion. These men, also, frequently do not present symptoms, their condition being discovered accidentally in the demobilization, after they have done full duty.

If aortic insufficiency exhibits itself by the presence of only a murmur, without other cardiac signs or cardiac symptoms, why should not any other cardiac lesion do the same? The murmur of aortic insufficiency is not simulated frequently enough by accidental or cardio-respiratory murmurs to warrant question of the diagnosis, provided the typical murmur is present. The chief difficulty in the diagnosis of other valvular lesions lies in the fact that the murmurs resulting from these lesions may be duplicated almost exactly by murmurs from other causes. The diagnosis of mitral insufficiency, for example, is often very difficult because of the variety of systolic murmurs that

may be heard over or about the apex of the heart; hence we often find ourselves obliged to decide the significance of a single cardiac phenomenon on its own merits.

This report is made for two purposes: first, to show the incidence of deviations from the usual found in heart examinations of healthy soldiers who have done duty, and second, to discuss the physical examinations of men with irritable heart in the light of the above data.

Thayer[1] has given his experience bearing on diagnosis of these phenomena. He describes as normal phenomena: (1) The systolic click; (2) the third heart sound; (3) basic systolic murmurs; (4) apical systolic murmurs which disappear in the erect posture, and (5) the cardiorespiratory murmurs. He classifies extrasystoles and reduplication of the second sound at the pulmonic area as phenomena the significance of which must be determined for the individual case. He considers them of no especial significance per se, but as confirmatory evidence of cardiac disease in certain cases in which other signs are present.

At U. S. Army Hospital No. 9 the most careful physical, laboratory and electrocardiographic examinations of soldiers with irritable heart have failed to show any organic defect in the heart. These men are, however, peculiarly apt to present adventitious phenomena in the heart, especially cardiorespiratory and "accidental" murmurs. The question arises whether such murmurs are purely accidental findings, or whether they have some bearing on the condition of the individual. Lewis,[2] after careful study of men with this complaint in the British Army, considers that the presence of cardiac systolic murmurs means nothing per se in irritable heart. He found that 58 per cent. of the men with this condition who were without murmurs were unfit for duty, whereas only 51 per cent. of the men with murmurs were unfit for duty. He found that 42 per cent. of all men with "soldier's heart" showed systolic murmurs. Possibly, the most direct way to approach this problem is by the examination of normal soldiers who have done duty. If all the physical findings of irritable heart are common in normal individuals, the inference should be allowed that such findings probably have no bearing on the condition of irritable heart.

While examining officers and men of the Air Service at Garden City for demobilization, I had the opportunity of studying and classifying auscultatory phenomena as they occurred in the hearts of healthy

1. Thayer, W. S.: "Observations on some of the commoner deviations from the ordinary met with in the examination of the heart of supposedly normal individuals," Med. Rec. **91**:617 (April), 1917.

2. Med. Research Committee Rep., 1918.

men who had done full army duty. These men were almost uniformly between 18 and 31 years of age, the average probably falling below 25. Five hundred men were studied in detail. The results of this examination are given in the table below. Two or more adventitious findings were not infrequently present in the same individual; the total number of men who showed one or more of the given sounds or murmurs was, therefore, somewhat less than the sum of murmurs and sounds found. In each case the man was examined in the standing, the supine and the left lateral posture. The effect of respiration on each murmur or sound was also studied.

AUSCULTATORY PHENOMENA OF 500 SUPPOSEDLY NORMAL HEARTS

	No. Cases	Per Cent.
Third heart sound	118	23.6
Reduplication of first sound at apex	16	3.2
Systolic apical click	2	0.4
Systolic murmur at apex present in recumbent posture, absent in erect posture	65	13.0
Cardiorespiratory systolic murmurs limited to inspiration:		
At apex	16	3.2
At conus arteriosus	4	0.8
At aortic area	3	0.6
Cardiorespiratory systolic murmurs present in both inspiration and expiration:		
At apex	13	2.6
At conus arteriosus	5	1.0
At aortic area	2	0.4
Accidental systolic murmurs:		
At conus arteriosus	70	14.0
At aortic area	31	6.2
Cardiorespiratory diastolic murmurs:		
Near aortic area	3	0.6
Near conus	1	0.2
Near apex	0	0.0
Extrasystoles	9	1.8
Reduplicated second sound at conus area	23	4.6

The Third Heart Sound.—On this point there is nothing to report, except the figures for healthy men in the third decade. Only well-marked third sounds are included. Third sounds heard for two or three beats after change of position and those heard for an occasional couple of beats during a certain phase of respiration were not recorded. Moreover, well developed men probably do not show the third heart sound so frequently as do individuals with thin chest walls. These two factors probably made the percentage lower than that reported by Thayer,[3] who heard this sound in 50.9 per cent. of individuals in the third decade of life. The sound was most often heard best with the patient in the left lateral posture, though occasionally it was loudest in the supine position. It was seldom heard distinctly in the erect posture. In no case was the sound associated with signs or symptoms of cardiac disease, and it was considered to be uniformly without significance.

3. Further Observations on the Third Heart Sound, Arch. Int. Med. **4**:297 (Oct.), 1909.

Reduplication of the First Sound at the Apex.—In this group are included cases in which two distinct and almost equally intense sounds occur at the very beginning of systole. Morris and Friendländer[4] have recently described this phenomenon in soldiers and have noted that it is sometimes associated with a short presystolic thrill and sometimes with a palpable double systolic impulse. They have pointed out that this condition may readily give rise to the erroneous diagnosis of mitral stenosis, and they consider the reduplication in itself as of no significance. They noted that it was heard best in the erect posture, disappearing entirely or being much diminished in the supine position. It is often very difficult to determine which of the two sounds is the louder; indeed, in some cases it is impossible to decide by auscultation. The reduplication bears no resemblance to the presystolic gallop rhythm nor to an auricular contraction; it is not similar to the "impure" or "flapping" first sounds. The two sounds are both forceful and distinct. There is, however, one distinctive quality of this type of reduplication, it either disappears entirely or diminishes in intensity when the subject assumes the supine position, being heard best with the subject erect.

In the series of sixteen cases recorded above, the reduplication disappeared entirely in ten cases when the man lay on his back. It has always impressed the writer as being due to the impact of the heart against the chest wall as it undergoes contraction and torsion during systole. This hypothesis is supported by the disappearance or diminution of the phenomenon in the supine posture, when the heart would tend to drop back from the chest wall. Occasionally the reduplication is accompanied by a distinct thrill; this occurred in two of the sixteen cases reported above. It has always seemed to the writer to accompany the systolic impulse, rather than to be really presystolic in time. The signs of this condition are radically different from those of mitral stenosis in the following respect. It is well known that the signs of mitral stenosis are usually maximal in the recumbent or left lateral posture; in these positions the signs of simple reduplication of the first sound are absent or minimal.

The Systolic Apical Click.—This was described by Thayer[3] as a single click or rattle occurring immediately after the first sound at the apex, of a wooden quality, superficial and sounding near to the ear, and seeming to result from the shock of the first sound. This click was heard not infrequently by me in the examination of some 15,000 soldiers. In the group of 500 reported here it occurred twice. It was

4. The Significance of Presystolic Thrills in the Examination of Soldiers, J. A. M. A. **71**:375 (Aug.), 1918.

always superficial, and seemed to result from the movement of the heart in its sac. It has been heard in early, late or mid systole. This click may become less distinct at the height of forced inspiration, but this is probably the result of the interposition of lung tissue from inspiration, for the sound fails to disappear at any phase of forced inspiration or expiration. It does, however, in some cases entirely disappear when the subject is supine, which strengthens the impression that it is an accidental extra-cardiac phenomenon.

Heart Sounds at the Left Sternal Border.—Blumer[5] described a crunching or scratching quality to the heart sounds in the region of the lower left sternal border. It is a common phenomenon of the normal heart, and may be observed in most hearts, in the leaning forward position particularly. Blumer considers that it probably originates in the tissues overlying the heart. He pointed out that the crunching quality is uninfluenced by respiration, that it is most marked in the leaning forward position, and that, in many cases, it is little or not at all influenced by change of position.

This phenomenon has been observed commonly by me in normal soldiers and in men with irritable heart. In two instances the scratching quality was drawn out and assumed the character of a true murmur. One of the cases occurred in a man with irritable heart, with vigorous heart action, who had been sent into the hospital with a diagnosis of mitral insufficiency. Examination showed the first sound at the lower sternal border prolonged into a definite superficial, squeaking murmur. This murmur, or squeak, was loudest in the leaning forward position. It was not influenced by respirations, but it was entirely absent when the man lay on his back. The location and characteristics of this murmur were so similar to the "crunching" quality of normal heart sounds, that it seemed almost surely to be a superficial friction sound of either the normal pericardium or of some of the other extracardiac superficial structures. Its accentuation in the leaning forward position was probably due to the friction of the heart against the chest wall, and its prompt disappearance in the recumbent posture probably due to the release of this friction.

In another case, a healthy nurse, with a perfectly normal heart and without cardiac symptoms, there was heard a short, early, very superficial, diastolic murmur along the lower left sternal border. It had none of the blowing quality of the murmur of aortic insufficiency, and it was obviously a superficial short "crunch" after the second sound, apparently due to the drawing out of the scratch of the second sound

5. A Note on the Normal Peculiarities of the Heart Sounds in the Region of the Sternum, Arch. Int. Med. **14**:605 (Oct.), 1914.

usually heard in this area. This murmur was not influenced by respiration; it was increased in the leaning forward position, and was least intense in the recumbent (supine) posture. This is a very rare phenomenon, and I did not notice such a murmur in the examination of about 15,000 soldiers. Nevertheless, on account of its occurrence in diastole and its position at the left sternal border, such a murmur might easily pass, on casual examination, for one of aortic insufficiency, and for this reason it is recorded.

It was noted that individuals who had "flat" chests, and especially those who had a tendency to "funnel-chest," usually showed the "cruch" to an unusual degree.

The Systolic Apical Murmur in the Recumbent Posture.—This is a common phenomenon, now widely recognized as an accidental murmur met with in normal hearts. It is second only to pulmonic systolic murmurs in frequency (see table). In the recumbent posture, the murmur has the quality of that of mitral insufficiency, but it differs from the murmur of true insufficiency by disappearing in the erect posture. It is not radically affected by respiration, as are the cardiorespiratory murmurs. It is never associated with cardiac hypertrophy or other secondary signs of cardiac disease in a causative rôle.

Cardiorespiratory Murmurs Limited to Inspiration. These murmurs are heard frequently, and should be recognized readily. If a murmur is limited to inspiration it may be classed at once in the cardiorespiratory group. They are most common at or about the apex, being often heard over the lingula pulmonalis or over the lung just outside the apex. They usually disappear promptly if a deep breath is taken and held at the end of inspiration. The explanation of this is simple, for the murmur is an intensification of the inspiratory lung sound, and when the lung is fixed at the end of inspiration it is not readily affected by the movements of the heart. Cardiorespiratory apical murmurs are most often loudest in the erect posture, thus differing from the accidental apical murmurs described in the preceding paragraph. They may disappear promptly when the subject assumes the supine position, probably from the dropping back of the heart and the release of pressure from the overlying lung. However, when the man assumes the left lateral position, cardiorespiratory murmurs are apt to reappear, probably because the heart swings toward the left and impinges on the lung again. Cardiorespiratory murmurs are often heard well in the left back, in which case the murmur seems to be formed in the lung behind the heart, and not to be transmitted from the apical region; cardiorespiratory murmurs are apt to be louder in the back than in the left axilla, probably for this reason.

Cardiorespiratory Murmurs Heard in Both Inspiration and Expiration.—These murmurs follow all the general rules of cardiorespiratory murmurs, as described in the preceding paragraph, except that they occur in both phases of respiration, usually disappearing when the breath is held at the end of full inspiration. The two varieties are almost equally common. One of the loudest murmurs heard in the cardiac wards of our hospital occurred in a man with irritable heart and belong to this group of murmurs. In the erect posture it was loud, rough, and lasted throughout systole; it was heard in the back, and occurred in both phases of respiration. When the man leaned forward, however, the murmur disappeared entirely, and it was also entirely absent in the supine position. It was clearly a cardiorespiratory murmur, for it could be made to occur even in the recumbent position by having the man take deep breaths; such a procedure would increase the volume of lung over the heart and restore the intimate contact of heart and lung. The disappearance of the murmur in the leaning forward position was interpreted as probably being due to the heart dropping forward and pushing the lung lappet aside.

Systolic Murmurs at the Base of the Heart.—These murmurs are discussed freely in the literature, and there is nothing to note except their frequency (20.2 per cent. at the aortic and pulmonic areas together). In the study of the 500 normal men, a heading had been set aside for "pulmonic systolic murmurs limited to expiration," as the elder Janeway[6] has pointed out the marked effect of forced expiration upon the pulmonary systolic murmur, and the writer had previously seen instances of this murmur's occurring only during expiration. However, in the group of men examined, no such case presented itself, though the murmur is almost always loudest after forced expiration. The murmurs noted at the aortic area were, in each case, similar to the pulmonic systolic murmurs in quality; there was no reason in any case to suspect valvular disease or aortitis, and the murmurs were considered as probably accidental.

Cardiorespiratory Diastolic Murmurs.—Occasionally superficial, to and fro, systolic and diastolic murmurs occur near the borders of the heart. Diastolic murmurs of this type may be distinguished readily from those of aortic insufficiency. The murmur may be limited to inspiration, in which case it may be classed at once in the cardiorespiratory group. It rarely occurs just at a valve area, and I have never heard it in the third left interspace, where the murmur of aortic insufficiency is usually maximal. In the four cases tabulated above it was always found just beyond the valve areas; in three cases it was

6. Discussion of Thayer's Paper, Trans. Assn. Amer. Physicians, **21**:61, 1906.

heard over the root of the aorta and in one case over the root of the pulmonary artery. These murmurs always disappear promptly at the end of forced inspiration. They are superficial, lack the blowing quality of the aortic insufficiency murmur, and are not transmitted. On hypothetical grounds, one might expect that a movement of air currents in the lungs could occur from relaxation of the heart and aorta in diastole as well as from the contraction of the heart and distention of the aorta in systole. Yet the occurrence of diastolic cardiorespiratory murmurs is not generally recognized. Almost certainly, however, any one can convince himself that they do occur by examining a sufficient number of healthy men. Such murmurs will seldom offer any serious complication, to a careful observer, in the diagnosis of aortic insufficiency, but the possibility of their occurrence should be borne in mind.

A Diastolic Murmur of Unknown Origin.—An endocardial murmur at the base of the heart or along the left sternal border that does not indicate aortic insufficiency is extremely rare. So far as I know, no such case was noted in the examination of about 15,000 soldiers. Cabot[7] described the cases of two medical students with "perfectly healthy hearts, who were able, by prolonged holding the breath, to produce a short, high pitched diastolic murmur, best heard in the second and third left intercostal spaces and ceasing as soon as the breath was let out." A patient seen recently at this hospital presented signs very similar to those described by Cabot. This man had a surgical and not a medical complaint, and the murmur was found accidentally. He had been a long distance runner. He gave no history of rheumatic fever syphilis, or other acute infection of importance, and the Wassermann reaction was negative. He had no cardiac symptoms. The heart was normal, but he showed a diastolic murmur along the left sternal border from the pulmonic area to about the fifth rib. It seemed to be an endocardial murmur, and it had the quality of the murmur of aortic insufficiency. It varied somewhat, in an inconstant way, on change of posture, but its most striking characteristic was the effect of respiration on it. When the man took a deep inspiration and held his breath, there was heard a high pitched, blowing, rather intense diastolic murmur along practically the whole left sternal border. As soon as he began to expire, however, the murmur began to decrease in intensity, and at the end of expiration, when the murmur of aortic insufficiency is loudest, this murmur was entirely absent. This case seems to be analogous to the two cited by Cabot, except that this murmur occurred during natural breathing, and would have com-

7. Physical Diagnosis, Ed. 6, William Wood & Co., New York, 1915.

pelled the diagnosis of aortic insufficiency were it not for its peculiar behavior at various phases of respiration. The cause of this murmur is unknown; in this case, it was not associated with any signs of heart trouble nor with any symptoms.

Extrasystoles.—Occurring in only 1.8 per cent. of the men examined for demobilization, extrasystoles are less common than they are in the examination of new recruits. They were not numerous in any case of the above group, and they never occurred with sufficient regularity to produce bigeminal or trigeminal rhythm. The heart was negative on physical examination in each case, and in no case were there any symptoms except palpitation.

Reduplication of the Second Sound at the Pulmonic Area.—This phenomenon was noted in 4.6 per cent. of the 500 men examined, and no significance for such reduplication could be found.

In the study of irritable heart at this hospital, no sounds or murmurs of the heart have been found which differed in any essential particular from the various types of murmurs described above as occurring in healthy soldiers who have done duty. There are numerous cardiorespiratory and accidental murmurs among men with irritable heart, but in view of the unusual vigor of the heart's action in such cases, it would be surprising if this were not the case.

SUMMARY

1. A report is made of the various adventitious sounds and murmurs found in the examination of the hearts of 500 supposedly healthy soldiers who had done army duty.

2. A few unusual murmurs and sounds found in the examination of almost 15,000 supposedly healthy soldiers are recorded.

CONCLUSION

Murmurs and adventitious heart sounds probably have only an accidental relationship to the "irritable heart of soldiers."

INFLUENZA AND NEUROSYPHILIS*

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Influenza has long been recognized as a precipitating factor in the production of mental disease. Although a few authorities maintain that it may be the sole cause of certain psychoses, probably no one today believes that influenza is ever the sole cause of general paresis. It has been observed, however, that neurosyphilis has sometimes appeared clinically for the first time after attacks of influenza, and this evidence makes the influence of influenza in the etiology of neurosyphilis a legitimate point of inquiry.

Even in the pre-Wassermann days influenza was, strangely enough, not generally considered as among the possible causes of general paresis. After the epidemic of 1890 a number of instances of the precipitation of neurosyphilis by influenza were reported, and these, along with analogous cases of epilepsy, chorea, etc., were styled by Kalischer,[1] Kirn[2] and others, "Pseudoinfluenza psychoses." The implication was that the influenza acted merely as an incidental precipitating factor and might be replaced by any other form of infection. Attention has been called to this repeatedly, and Duke[3] emphasizes the importance of peridental infections. It would seem that simultaneous infective processes may cooperate in their attacks on the system, producing a clinical picture, however, wholly resembling the usual results of the one assailant. At least, this is apparently the result in the case of the interaction of neurosyphilis and influenza.

A considerable number of instances of neurosyphilis appearing first after influenza were studied in the recent epidemic in the series reported from the Boston Psychopathic Hospital. In practically all of

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*A contribution from the Boston State Hospital, Psychopathic Department, Series of 1919. This is the third of a series of papers on Psychoses Associated with Influenza. The first appeared in J. A. M. A. **72**:235 (Jan. 25), 1919. The second has been accepted for publication in the Archives for Neurology and Psychiatry.

1. Kalischer: Arch. f. Psychiat. **29**:

2. Kirn (insists on this point in various of his several writings on influenza, e. g.), Ueber Influenza Psychosen, München med. Wchnschr. **37**:299, 1890. Die nervoesen und psychischen Stoerungen der Influenza, Samml. klin. Vortr., n. F., Leipzig, No. 23, 1891. Die Psychosen der Influenza, Allg. Ztschr. f. Psychiat. **47**: 1, 1891.

3. Duke, W. W., Oral Sepsis in its Relationships to Systemic Disease, St. Louis, 1918.

these cases there was close chronologic association of the influenza and the appearance or aggravation of mental (neurosyphilitic) symptoms.

The question is immediately asked as to the relationship of the influenza and the neurosyphilis. Is it more than that of chronologic sequence, more than coincidental? Is it a further manifestation of the neurotoxic potentialities of the influenza toxin? Is the effect confined to augmentation and never to alleviation of neurosyphilitic symptoms? To all of these queries the evidence at hand favors an affirmative answer.

LITERATURE

Of the literature concerning the relation of influenza to neurosyphilis, there is a remarkable paucity. Leichtenstein,[4] in his celebrated monograph covering the subject intensively, confines his consideration of neurosyphilis to this sentence: "The first signs of 'general paralysis' have often followed influenza (Althaus[5])." Leledy[6] lists three cases, one of his own, one quoted briefly from Kraepelin, and a third from Magnan's clinic, reported by Rabinovitch. All three are cases of neurosyphilis paretica, appearing in an acute form first after an attack of influenza. Mills[7] and Knapp[8] concluded that at least as far as paresis was concerned, "influenza only reveals old syphilitic processes or exaggerates some troubles which previously had passed unperceived."

Krypiakiewiez[9] cited a case "in which" (comments Espagnol[10]) "the relation of cause and effect between general paresis and influenza seems very close."

Erb,[11] in discussing tabes, wrote that ". . . it is certain that if influenza be added to tabes it decidedly aggravates the affection and accelerates its cause, and there is no doubt that the first tabetic symptoms occasionally appear after an attack of influenza." But he appends a note of skepticism as to the possibility of influenza as a sole cause.

But, in general, the literature is very scant, probably the most so of any phase of the psychiatric side of influenza. Bossers,[12] in his

4. Leichtenstein, O., Influenza, Nothnagel's Encycl. **103:**
5. Althaus, Am., J. M. S. 361, 1892.
6. Leledy, A., La Grippe et Alienation Mentale, Paris, 1891.
7. Mills, Trans. Phila. Co. Med. Soc., 1892.
8. Knapp, P. C., Boston M. & S. J., 1891.
9. Krypiakiewiez, Jahrb. f. Psychiat., **10:**
10. Espagnol, J., Contribution a l'étude des rapports de la grippe et dû systéme nerveux, Toulouse, 1895.
11. Erb, Deutsch. Klinik, edited in English by Church, Appleton's Modern Clinical Medicine, New York, 1908.
12. Bossers, A. J., Die Geschichte der Influenza und ihre nervoessen und psychiatrischen Nachkrankheiten, Leiden, 1894.

excellent monograph, does not mention it. No articles dealing directly with the subject were found in a search of the Surgeon-General's Index, the Ind Medicus, and the bibliographies of such monographs as those of Bossers,[12] Bonhoeffer,[13] Leichtenstern,[4] Espagnol,[10] etc. It is not mentioned in Nonne's[14] authoritative work, nor by Southard and Solomon[15] in their case-history book, and these are certainly our best modern treatises on neurosyphilis.

The following case histories of neurosyphilis were taken from the series of cases of mental disease associated with influenza observed at the Boston Psychopathic Hospital in the recent epidemic.[16] They fall logically into four groups, with a fifth hypothetical group not illustrated. The groups have, as a basis of classification, the degree of pre-existent symptomatology, and are explained in the text.

CASE HISTORIES

GROUP 1.—Cases in which there were no symptoms of neurosyphilis whatever until after the attack of influenza.

CASE 1.—*Normality + (Latent Syphilis) + Influenza = General Paresis.* Male, aged 46, single, contracted influenza followed by irritability, delusions, amnesia, dysthymia. The serology and neurology was that of neurosyphilis paretica.

(It is certain that not many years ago the circumstantial evidence of such a case as this would have been accepted as proof of the possibility of a non-syphilitic etiology for general paresis.)

Family History.—Negative.

Past History.—Negative. The only symptom of any kind prior to an attack of influenza had been the complaint of fatigue during the four preceding summers. He used no alcohol or tobacco.

Present Illness.—He contracted influenza, which became rather severe in degree but terminated in four days. He arose from bed, but evidently suffered a relapse and returned to bed again, after two weeks. Two days following this he was delirious. He is also described as being irritable and negativistic, and announced that the Blessed Virgin Mary was going to tell him what to do. There is a vague account of two seizures. He was then brought to this hospital.

Mental Examination.—His consciousness seemed entirely clear. He was correctly oriented, but with a grossly defective memory for both recent and remote events. He presented fleeting persecutory somatic delusions, fearing that he was dying, that he had been poisoned, etc. No hallucinations were elicited. His emotional tone showed instability and at times a tendency toward agitated depression. There was a disruption of thought processes and a decrease of motor activity.

Physical Examination showed no defect of special senses or of epicritic or protopathic sensations. Deep sensations were somewhat impaired. The pupils

13. Bonhhoeffer, Aschaffenburg's Handb., Leipsig & Vienna, 1915. Menninger, Karl A., Psychoses associated with influenza, J. A. M. A. **72**: 235 (Jan. 25), 1919.

14. Nonne, Syphilis of the Nervous System (translated by Ball).

15. Southard & Solomon, Neurosyphilis, Boston, 1917.

16. Menninger, Karl A., Psychoses associated with influenza, J. A. M. A. **72**:235 (Jan. 25), 1919.

were contracted and reacted neither to light nor accommodation. Tremor of facial muscles, tongue and extended hands was present. The knee jerks were equal and active. There was slight swaying in the Romberg position. The abdominal and cremasteric reflexes were absent.

The blood serum Wassermann test was positive. The spinal fluid showed an increase of albumin, globulin, four cells and a unique gold sol reaction of 5555555555, with a positive Wassermann reaction.

Diagnosis.—Neurosyphilis paretica (general paresis). The man was committed.

CASE 2.—*Normality + (Syphilis) + Influenza = Cerebral Syphilis.* Male, aged 31, salesman, who had had chancre eleven months previously, now had a severe attack of influenza, with "delirium" and seizures. The spinal fluid findings were typical of paresis, except for a negative Wassermann reaction.

Family History.—A brother is considered "mentally undeveloped;" otherwise the family history is entirely negative.

Past History.—This is entirely negative, except that he formerly used considerable alcohol, but was never drunk or hallucinated, and had been for six months totally abstinent. He had been quite successful in business, and earned a substantial salary.

Marital History.—He was married eight years prior to admission; his wife is living and well but childless because of a hysterectomy done prior to marriage.

Present Illness.—He admitted that despite his happy married life, he had been on several occasions unfaithful to his wife. Three years previously he had had gonorrhea and one year—he thought precisely eleven months—previously he had had a running sore about the size of a dime on his penis, which was not particularly painful or indurated. It disappeared after about three weeks and was not followed by adenitis, pharyngitis or dermatitis. He did not consult a physician. The scar remains.

For the past five years he has had "grippe" every year. December 12, 1918, while traveling across country by automobile, he was taken with a severe headache and general malaise. He arrived home at 10 p. m. with a temperature of 103.5 F. A physician was called and diagnosed his case as one of influenza.

December 15 (third day) he had "what appeared to be a convulsion" (physician's written statement). Involuntary urination occurred, and "he seemed to be dying." The attack lasted about five minutes. He had no memory of it afterward, and asked his wife why she appeared so frightened. Later in the day he remarked to her, "I think I fainted again," but there was no proof of this.

December 19 (seventh day) his temperature fell to normal. In the morning he related some bad dreams of the night before, and later in the day he spoke queerly and somewhat incoherently. At 7 p. m. he had another convulsion, "all his limbs contorting, he frothed at the mouth and beat the air with his hands." He appeared frightened, and what he said could not be understood. "His wife had great difficulty in holding him in bed. The attack lasted about five minutes."

Following this attack he did not regain consciousness fully, but remained "stuporous and queer," obeying a few commands, signalling for the bedpan and keeping himself covered, but unable to speak intelligently.

December 17 (ninth day) he entered the hospital in a state of delirium, disoriented and oblivious to external stimuli. Pupils then reacted poorly to light. He muttered an unintelligible jargon and tossed about on his bed incessantly.

December 18 his condition was unchanged during the forenoon. About 10 a. m. a lumbar puncture was done, and thereafter he became quite clear, approximately oriented and, on the whole, fairly normal mentally.

December 19 (eleventh day) he was quite clear until about 10 a. m. His mentality became greatly retarded, then completely blocked. This was followed by a severe seizure, tonic convulsions with cyanosis, champing bloody froth and

gross tremor, succeeded by clonic spasms for several minutes and then stertorous coma.

For a short time afterward he was in a typical "twilight state," fabricated freely, and was completely disoriented. Fifteen minutes later he was entirely clear and entirely amnesic for the seizure. The same afternoon he had another seizure of much less severity.

December 20 and 21 he remained entirely clear. A routine mental examination was in all respects entirely negative except for an undue euphoria. He begged with spirited earnestness to go home for Christmas, talked somewhat too loudly, but passed for entirely normal with the whole staff. He was discharged against the advice to his wife on December 22. No more seizures occurred.

Physical Examination.—Pupillary reaction was sluggish to light on admission, but subsequently responded normally. All reflexes were normal, and there were no abnormal physical or neurologic findings. There was a scar, like that of a chancre, on the glans penis. The blood pressure was 120-70.

Laboratory Findings.—The urine was negative. Blood examination showed 4,700, 000 erythrocyts, 12,900 leukocytes; hemoglobin, 80 per cent. The differential white count was normal. Spinal fluid examination showed globulin 2 plus, albumin 2 plus, forty-one cells, of which nine were small and eighteen large lymphocytes, and fourteen were polymorphonuclear cells. The gold sol reaction was 5554321110. Wassermann tests of spinal fluid and blood serum were negative. Diarsenol G., 0.3 gm. had been given on the fifth day. The psychometric rating on the sixth day was 11.4 years.

Diagnosis.—Neurosyphilis (cerebralis: ? paretica).

CASE 3.—*Normality + (Latent Syphilis) + Influenza = General Paresis.* The patient was a man, aged 40. His wife was known to have had syphilis. No nervous manifestations were noted until after an attack of influenza. It was a typical paresis.

Family History.—This was negative, including the grandparents.

Past History.—Childhood was normal and his past life was negative. He had worked at various trades, but for fifteen years had conducted his own barber shop successfully. His wife had no miscarriages but is known to have had symptoms of syphilis many years previously. Two children are living and well. His habits had been quite good, and he was not alcoholic. There had been no serious illnesses.

Present Illness.—The man had been perfectly well in every respect. The previous year he had made more money than ever before, clearing over twelve hundred dollars from his barber shop and the few side affairs. He was extremely sociable, was perfectly well, both physically and mentally, according to well authenticated reports.

Some time in October he had had influenza for four days, his temperature rising to 103 F. It was not considered a particularly severe attack. He returned to work at once, but felt it a great exertion. From then on his wife noticed that he was unusually quiet and averse to conversation, which was quite in contrast to his former state. He began to show signs of memory difficulty and complained of it specifically. He did not, however, show any more severe symptoms for six months.

May, 1919, he was involved in some unjust legal difficulties. In the evening he came home very much disturbed. His wife states he was extremely restless, emotionally unstable, manifested twitchings in various parts of his body and constantly uttered complaints and laments. On the advice of his physician he came to the Psychopathic Hospital.

Mental Examination.—This showed pre-eminently a variable emotional tone, exhibiting in succession threats, laughter, tears and song. He was quite euphoric the greater part of the time, and alternated protestations of the excellence of

his health with complaints that he was still sick with the influenza from which he had never really recovered. There was marked psychomotor restlessness with great loss of attentive control. His memory was not markedly defective and hallucinations were not proved although both auditory and visual hallucinations were mentioned. Impairment of judgment was manifested in various minor ways; as, for example, in outbursts of profanity and obscenity before nurses, harangues of advice to other patients, threats of violent suicide, etc.

Physical Examination.—This was chiefly negative, including the routine neurologic tests. His pupils, however, reacted through a small arc, and there was considerable flattening out of the face.

Laboratory Findings.—The urine was negative. The blood Wassermann was negative. The spinal fluid was positive. Wassermann positive, with an increase of albumin and globulin, 163 cells, and a gold sol reaction typical of paresis (5554321000).

Diagnosis.—Neurosyphilis paretica.

CASE 4.—*Normality + (Latent Neurosyphilis) + Influenza = General Paresis.* A man, aged 51, formerly a naval officer, after an attack of influenza, became "mentally foggy," demonstrated to be due to general paresis.

Family History.—Entirely negative.

Past History.—Chiefly negative. He was born in Maine, spent nearly 40 years at sea, part of the time as a high ranking naval officer. He had a common school education, and had had typhoid fever in childhood. He was mildly alcoholic, but had an excellent personality. He married at 32, and has one living child.

Present Illness.—November 6, 1918, he contracted influenza and was in bed for ten days. Absolutely nothing wrong had been noticed prior to that time. Thereafter a speech defect first appeared, then he was noticed to be becoming forgetful and irritable, and later destructive. He became more and more "foggy" and demented and was admitted to this hospital March 24, 1919.

Mental Examination.—At the time of admission he showed a grossly defective memory with absolutely no insight, and slight euphoria. His psychomotor activity was somewhat increased. He was quite restless a great part of the time, and occasionally he was destructive. There were no delusions or hallucinations. His thought processes showed retarded cerebration and considerable decimation. Most of the time he was disoriented.

Physical Examination.—This showed excellent development and nourishment, and no somatic pathology other than the neurologic examination, except what was diagnosed a gumma of the epididymis. Neurologic examination showed small pupils, which though equal did not react to light. There was a positive Romberg, with tremor of the tongue and hands, and all the deep reflexes were exaggerated. Ophthalmoscopic examination was negative. Speech defect was quite prominent.

Laboratory Findings.—The urine was negative, likewise the blood cytology. The blood Wassermann (three tests) was positive. Spinal fluid contained globulin and the albumin was much increased; eight cells. The gold sol test gave 5 5 5 5 5 5 5 4 2 2. The psychometric test gave a rating of 8.5 years.

Diagnosis.—Neurosyphilis paretica.

NOTE: He was immediately put under treatment. Received potassium iodid daily and diarsenol brand of arsphenamin bi-weekly. By the end of a month the tumor of the epididymis had decreased in size, speech had improved, he had begun to take a little interest in things and was generally regarded as having improved.

CASE 5.—*Normality + (Latent Neurosyphilis) + Influenza = General Paresis.* A male, aged 47, who, prior to an attack of influenza, had been perfectly well, thereafter developed symptoms of general paresis.

Family History.—Negative.

Past History.—He was born in Ireland, had a normal childhood, and has been fairly efficient economically since coming to the United States, earning twenty-five dollars a week as a waiter. He has been married for six years and has one child, with no miscarriages, no stillbirths and no dead children.

Present Illness.—It is established that prior to his influenza he was considered quite well and manifested no symptoms, mental or physical.

In October, 1918, he had influenza with a maximum temperature of 102.6 F. and was in bed for five days. He returned to work and was considered quite well for about a month, except that his wife thinks he was "nervous." January 1, however, he lost his position and from then on was noted by several people to be "not himself," and as he himself put it, in March, "all in." At this time he became disoriented and "childish" in his talk. He manifested difficulty in verbal expression of his ideas and suffered from insomnia. Memory defect was also noted.

Mental Examination.—On admission to this hospital, April 1, he was found to have a considerable bewilderment of thought processes, disorientation, memory defect, with an emotional tone of apathy and torpor. He lacked insight totally, and showed a speech defect.

Physical Examination.—This was chiefly negative. There was some evidence of chronic pneumonitis of the left upper lobe. Neurologically, the deep reflexes were all exaggerated and the periosteal reflexes were marked. Otherwise, the examination was negative.

Laboratory Findings.—The urine was negative. The blood cytology was normal. Serology showed a positive Wassermann. The spinal fluid findings were increased globulin and albumin, forty-eight cells, of which forty were small and eight large lymphocytes, and a positive Wassermann. The gold sol reaction was typically paretic, viz., 5555554420.

Diagnosis.—Neurosyphilis paretica.

GROUP 2.—Cases in which the previous symptoms were trivial, and not diagnostic, but in which typical and advanced neurosyphilis developed immediately after influenza.

CASE 6.—*(Latent Neurosyphilis)* = *Paranoid Personality* + *Influenza* = *Advanced Neurosyphilis* (paretica). A woman, aged 39, paranoid for several years, during convalescence from influenza suddenly manifested profound dementia (paralytica).

Family History.—Negative, including grandparents.

Past History.—Normal childhood and school life. Wages steadily advanced to $183 a month. "She is the brightest woman in the Chamber of Commerce and very much valued." She was married at 19 years of age to a shoe salesman, who is 41 years of age, living and well. One child is living and well. She had no miscarriages. She does not use alcohol. Her sexual habits are normal. Her medical history is negative. She has not had any previous illnesses.

Present Illness.—The history is repeated as given by the husband who seemed to be an intelligent and reliable informant. Four or five years ago the patient began to find her work difficult, and she began to lose weight. She was noticed to change in disposition, becoming tired, irritable and easily upset. She was annoyed by trifling things, such as careless dressing of strangers. This tendency increased and six months ago she began to be suspicious of her fellow workers. She said that the other girls talked about her, laughed and looked at her hair and at her clothes. This she put down to the fault of the woman who was at the head of them, who, for some unknown reason, was "down" on her. This woman had been a friend of hers. She also had ideas of reference on the street. All this took place despite the fact that her work was of excellent quality and her wages had been increased.

She took a two weeks vacation in August, at which time she had a bad headache, which lasted a month. She was given medicine and it went away. August 17 she contracted influenza and was in bed for five days. She had a fever but was not delirious. She recovered, but was advised not to return to work until the end of the week of admission. September 25 she was apparently as well as ever, and had taken a walk on the day before. She was not at home in the evening when her husband returned from work. Search for her was in vain. She was not seen until the next day, when she was found in the park on the grass, wet to the skin, with her hair down. She stared at her husband and could give no account of herself. She seemed to be unable to speak. At night she seemed to be trying to tell him something, but could not get it out. She kept saying "yes" repeatedly, and waved her arms as though someone was chasing her. The only coherent sentence she made was that she had brought her hat home anyway. She did not sleep that night, but kept repeating, "I am going to get rest" and rubbing her eyes. She seemed to be totally disoriented for time, place and person.

Mental Examination.—The patient, when brought to this hospital, gave a scattered account of herself with mention of the various factors related by her husband in an incoherent, straggling fashion, grimacing as she spoke and showing great emotional dullness. She was approximately oriented at that time. Mental examination was somewhat hampered by her retarded ideation and sluggish thought processes. Her consciousness was not clouded. Her memory was very defective in the characteristic patchy manner. Thus, although she could give correctly simple items of school knowledge, she could give no account of her illness and a very incomplete account of her past life. There were no delusions or hallucinations, nor, on the other hand, any insight. Thought processes showed attention rapidly gained, but retained with difficulty, retarded flow of ideas and slow, incoherent associations. She initiated no conversation. Her emotional tone was distinctly dull and apathetic. Her conduct was quiet and aboulic. She grimaced a great deal, especially accompanying her speech. There was a slight speech defect. Her condition did not change in any respect during her stay here of ten days.

Physical Examination.—The patient was a fairly well developed and nourished white female, quiet and cooperative, with an entirely negative physical examination except for mildly hyperactive knee jerks, a doubtful Babinski on both sides, and pupils which were irregular, unequal in that the right was slightly larger than the left, and a reaction as follows: "Both react slowly and through a narrow arc to light, the right one being more sluggish; reaction to accommodation normal." The blood pressure was 100-50.

Laboratory Findings.—The urine was negative. Vaginal and urethral smears were negative. The blood Wassermann was positive. Spinal fluid examination showed globulin ++, albumin ++, cells 121 (99 small lymphocytes, 19 large lymphocytes, 3 neutrophilic polymorphonuclears). The gold sol reaction was 5555444430.

Psychometric Test.—The patient graded slightly irregularly with a variation total of twelve, at a mental age of 8.8 years. The performance on the construction puzzles was poor, and on the memory tests very poor. In the suggestibility test she accepted six out of ten suggestions. She cooperated well and seemed interested.

Diagnosis.—General paresis (neurosyphilis paretica). The patient was committed.

CASE 7.—*Cyclothymia + Alcoholism + Influenza (+ Syphilis) = Paresis.* This was a harlequin case of very unusual features. The patient was a male, aged 61 years. He had had many commitments for cyclothymic and alcoholic psychoses. He was apparently normal for a time, then influenza, and thereafter an acute psychosis disclosed a general paresis. This man was born in

New Brunswick. His parents were born in Ireland. Nothing more than this is known about the family history.

Past History.—The patient's past history is largely a record of his successive commitments. Nominally, he was for the most of his life a common laborer in the saw mills and woods of the north; actually he spent much of the time in various state and provincial hospitals.

At the age of 23 he was committed to a provincial hospital in Canada with the conventional diagnosis of "melancholia." Thereafter he was probably committed numerous times, but no records could be secured until his commitment to a state hospital in Maine at the age of 52, because of conduct disorder accompanying agitation and depression. Thereafter he was committed time after time, in each instance with the same symptomatology, and usually the same diagnosis, "Manic depressive insanity, depressed phase, with alcohol as an exciting factor." Alcoholic hallucinations was diagnosed twice. The symptoms would abate in from two to six months, and he was never kept longer than the latter period. He is known to have been committed fourteen times, and the actual number of commitments is probably considerably greater.

"Diminished knee jerks" is the only evidence of nervous pathology offered by the clinical records of the hospitals where he was committed. Apparently laboratory tests were not made.

Present Illness.—For eighteen months he had been free from any mental symptoms, having been discharged then from a state hospital with the diagnosis of "alcoholic hallucinosis." (He had been deluded, hallucinated, depressed, retarded and self-accusatory. On a priori reasoning the diagnosis is certainly open to some doubt.) He had been working (and drinking) steadily until three weeks before admission when he contracted influenza. It is not known exactly how long he was ill. He was in the hospital of the Falls River ship building plant. About a week after his discharge therefrom, he began to be talkative in an irrelevant, incoherent and unintelligible manner. Typical of this is his reply to the question in the admission office, "Have you delirium tremens?" which was . . . "It was upset in the bag. I have heard them talking all day." He readily accepted the suggestion that he had been doped, and went willingly (although vociferously) to the ward.

Mental Examination.—A routine mental examination was never possible as he was completely inaccessible and uncooperative. He wandered constantly about the ward, jabbering in a monotonous voice an endless rigmarole. His replies were irrelevant, incoherent and meaningless. Attention could be gained for a moment but it was impossible to hold it longer. His ideation and thought content could not be determined, or his memory tested, because of his desultoriness and irrelevancy, but he seemed at times to be correctly oriented for time and place ("state hospital"). His conduct disorder consisted in a multitude of trivialities, uncleanliness, denudativeness, removing his clothes and washing them in the hopper, wiping his face with his socks, ruffling the bed, etc. He showed no tendency to violence. His emotional tone was that of a mild euphoria, with a rather general indifference to most of his environment. He was probably constantly hallucinated.

Physical Examination.—He was a well developed and well nourished man, rather bald, with no anomalies or malformations. The general physical examination was entirely negative, save for a harsh systolic aortic murmur, with evidence of considerable peripheral arteriosclerosis. The blood pressure was 130-60. The neurologic examination was negative, including the ophthalmoscopic, except for a fine tremor of the hands and diminished knee jerks. Coordination could not be well tested, but seemed poor.

Laboratory Findings.—The urine was negative. The blood serum Wassermann was positive. The spinal fluid Wassermann was negative (!). The spinal fluid globulin and albumin were normal (???,KAM); 56 cells. The gold sol reaction was 5544443200.

Diagnosis.—The man was committed with the unqualified diagnosis of neurosyphilis paretica (genera paresis). (The staff presumably, and I certainly, agree heartily with Hunt's[16] recent dictum, "The gold test is the one of all most to be relied on."

One of the interesting facts about this case is the unusual combination of alcoholism, syphilis and cyclothymic psychosis with the precipitation of badly demented paresis by an attack of influenza. A second remarkable thing is the absence of neurologic signs in the presence of so manifestly advanced paresis. A still further remarkable fact, and one which may be contested by a few, is the rather equivocable laboratory findings in the spinal fluid. Not only is it unusual to have normal albumin and normal globulin with general paresis, but the concomitant finding of fifty-one cells makes the examination open to doubt. The gold sol reaction is quite typical. The negative Wassermann, while quite unusual, is not at all without precedent.

NOTE.—At the state hospital to which he was committed he showed quite a different picture within the next few months and developed additioned symptoms. The left ankle jerk disappeared, the right became sluggish. A contralateral adductor response was elicited on both sides. Pupils and speech remained normal. Mentally he is described as being defective in orientation and recent memory, dull and apathetic emotionally, and "harboring vague ideas of self accusation, reference and fear." The diagnosis made there (in the absence of serology reports) was split between dementia paralytica, dementia praecox, dementia senilis (arteriosclerotica) and dementia alcoholica.

GROUP 3.—Cases in which the previous symptoms were diagnostic of mental disease (nervous syphilis) but were intensely aggravated (to a committable degree) by the influenza.

CASE 8.—*(Syphilis +) Queerness for Several Years + Influenza = Advanced Paresis.*—A male, aged 40, for some years considered queer, recently became troublesome. He had influenza, followed by visual hallucinations, disorientation, amnesia, etc.

Family History.—The patient was one of twenty-two children, of whom all but seven died in infancy or youth. The mother also had several miscarriages. His father had twenty-seven brothers and sisters, and the mother an equally surprising number (exact figures not known). There is no history of mental or nervous disease.

Past History.—His childhood was uneventful. He left school to begin work at 14 and worked in shoe factories thereafter. His maximum earnings were $36 per week. He was married twenty-three years previously to a French Canadian woman. It was not a very happy marriage. He has eight living children. His wife had no miscarriages.

Present Illness.—(Paraphrased from the physician's written statement and the history furnished by wife, sister and father). For several years he had been acting queerly at times, such as "talking loudly to himself when alone, asking questions as if talking to other persons and giving the answer himself." Recently he had seemed tired and complained of headaches. Two weeks before Christmas he assaulted his daughter, striking and injuring her. Christmas day the doctor was called and diagnosed influenza. His temperature fell to normal

16. Hunt, E. L.: Some Practical Points in the Diagnosis of Syphilis of the Nervous System, Med. Rec. **95**:393 (March 8) 1919.

January 2. January 1 the patient had seemed more queer than ever. He reacted to hallucinations for about an hour in the afternoon. This recurred the following day, with a normal temperature, and again thereafter. He would speak of the (imaginary) child he was holding, direct his wife to pull (an imaginary) chain from the ceiling, etc. He began to mistake identities, called his wife by a wrong name, imagined "every day to be Sunday," thought himself in a western Massachusetts town, etc. He also began to be disturbed and unruly at night and finally was brought to the Psychopathic Hospital, "his lucid intervals growing shorter and less frequent."

Mental Examination.—He was a dull, apathetic man, aged 40, but appearing older, who answered in a low, indistinct voice without any attempt at cooperation. He was grossly disoriented, especially in the temporal sphere. His memory showed a severe grade of deterioration, there being almost no coherent memory for either recent or remote events. He could not remember when he was born, whether or not he attended school, who was president, etc. Characteristic of his disorder, he recalled and gave correctly some minor but complicated facts such as the list of New England states, etc. While no delusions or hallucinations were elicited, he had absolutely no insight, and did not understand why he was in a hospital except that he "had some diarrhea" or "was dizzy last week." His thought processes showed utter decimation; his attention was fleeting; his associations were loose and weak; his train of thought broken and incoherent. His emotional tone was that of complete indifference. Any expression of emotion that he did give was obviously only verbal. His motor status was in general characterized by inactivity, aboulia, hypokinesis. At times he got up and wandered about the ward, becoming lost, and requiring to be led back to his bed or chair. There was a very slight speech defect, frequently, but not always detectable. Much more prominent was the low, indistinct, disinterested manner of speech, representative of his severe dementia. He did not change in any material way.

Physical Examination.—(Summary.) A well developed and nourished man, aged 47. He has no subjective complaints. Smell, vision, hearing, taste, sensation, gait, station, speech and all reflexes are normal. There are no paralyses, clonuses, atypical reflexes, atrophies, vasomotor disturbances, etc. The pupils are equal but irregular; they react through a narrow arc, but promptly, to light. The blood pressure is 130-75. Physical examination is otherwise negative.

Laboratory Findings.—The urine is negative. The blood serum Wassermann is positive. The spinal fluid showed globulin ++, albumin ++, 17 cells (15 small and 2 large lymphocytes) and a gold sol reading of 2223220000.

Diagnosis.—Neurosyphilis (paretica).

GROUP 4.—Cases of neurosyphilis in which the clinical manifestations and course were not perceptibly influenced by the influenza.

CASE 9.—*Tabes Dorsalis, Arrested, + Cyclothymia + Influenza = Cyclothymic Psychosis (Neurosyphilis Unaffected).*—A male, aged 52, clerk, married, had tabes, the result of syphilitic infection at 18. There was good response to treatment; the symptoms were arrested. He had influenza followed by a typical episode of manic depressive insanity of the depressed phase. The syphilis manifestations were unaltered.

Family History.—Negative.

Past History.—His childhood was essentially normal. He went to school from the age of 6 until 18, completing two years in a university. For twenty years he has been clerk for a railroad at $34 a week.

His habits have been regular for many years. He drinks one or two whiskies daily, but is never drunk. In 1892 he married a woman who proved to be alcoholic and immoral. He has been divorced for twenty years. Two children are living and well. His wife states that he was apparently dis-

tinctly subject to melancholia, humors, moods, but without previous psychotic episodes. He had pneumonia thirty-two years previously and contracted gonorrhea and syphilis at the age of 18. Treatment at that time consisted of mercury pills. He was treated at the Peter Bent Brigham Hospital, to which hospital I am indebted for the following abstract:

June 30, 1917. Patient admitted to the hospital. For the last three or four years the patient has been incontinent of urine, has been conscious of a constricting sensation about the waist, and has had irregularity of the size of the pupils. For two years vision has been gradually failing with diplopia in looking at distant objects, unsteadiness of gait and difficulty in walking in the dark. The pupils are unequal, irregular and do not react to light. There is marked impairment of vision of the right eye, there being no vision on the nasal side. The inguinal glands are distinctly enlarged. The knee jerks are absent and the Achilles and plantar reflexes are diminished. The gait is ataxic and the Romberg sign is present. The Wassermann and spinal fluid are positive.

July 20, 1917, the spinal fluid showed forty cells and a globulin ++. He received one intravenous and one intraspinal injection of diarsenol. He has also received intramuscular injections of mercury succinamid. The pupils are fixed; the knee jerks are absent. Discharged. Diagnosis. Tabes dorsalis.

Patient was admitted at various intervals, a total of ten, for treatment. His last admission was Sept. 14, 1918. Physical examination at that time showed the right pupil smaller than the left. Both are fixed. The knee jerks are absent. The muscle sense is good. He sways slightly in the Romberg position. The spinal fluid shows eight cells and a slight possible trace of globulin. The Wassermann is ++. Discharged Sept. 15, 1918. Diagnosis: Syphilis; tabes dorsalis.

Three months prior to his admission here he reported at the Brigham Hospital and was told that his spinal fluid showed no signs of syphilis. Since that time he had had a second test which was also negative.

Present Illness.—Four weeks prior to admission he developed influenza (October 4), and was in bed for several days. He had not felt well since and did not return to work. The night before admission (October 31) he became excited, insisting on telling his relatives about his condition—that he had syphilis and would never get well. He insisted that he was "all in," in a dreadful condition, that his case was entirely hopeless, etc. He described a great many symptoms which he actually did not have, and had not had for some time, such as urinary incontinence, and insisted that his bowels had not moved for weeks.

Mental Examination.—The patient entered expressing ideas as indicated above, but without hallucinations and without any impairment of memory or intellectual processes. This was accompanied by depression and at times apprehension and agitation. His thought processes were retarded, but not greatly, and his motor status was normal. Following the lumbar puncture he was even more depressed. "Thinks that his tabes has advanced to such an extent that nothing ever can be done for him." Later he decided that he was growing much worse, that he was to die very soon, and feared that he might start a pestilence here. He decided he could detect uriniferous odor about himself.

Physical Examination.—The patient was poorly developed and badly nourished, complained of paresthesias, but showed no evidence of physical disease, except neurologic findings which were as follows: The special senses and sensation were normal; the muscle sense was good. There was no vasomotor disturbance. Moderate atrophy of leg muscles was present and evidence of an old fracture. The ocular movements were normal. There was no ptosis, nystagmus or strabismus. The pupils were dilated, equal and round; reaction to light and distance was absent. The pharyngeal reflex was present. The cremasteric reflex was not obtained. The knee jerks were absent. His gait was unsteady. The Romberg was positive. Coordination was poor. No

Babinski or clonus was present. The periosteal reflex was absent. There was essentially no change in his condition.

Laboratory Findings.—The urine was negative. The spinal fluid showed globulin +, albumin +, two cells. A sensitive gold sol reaction read: 0111233430. The Wassermann reaction was positive in the first three dilutions. The serum Wassermann was not reported.

Ophthalmoscopic examination showed an old optic atrophy of the right eye and a normal left fundus, except for a very heavy pigmentation.

November 25, twenty-five days after admission, he was transferred to another state hospital with a diagnosis of depression with tabes. The minority of opinion favored the diagnosis of manic depressive insanity, depressed phase.

I do not regard the neurosyphilitic process as having been manifestly altered. The psychotic episode passes very well for the depressed phase of a cyclothymic psychosis, although depression with tabes is a recognized syndrome which might be defended vigorously. Perhaps it is wrongly classified here, but if so it deserves a class for itself.

CASE 10.—*Congenital Neurosyphilis + Influenza = No Change.* A female, aged 21, with congenital neurosyphilis, had hemiplegia for five years and seizures for two years. Influenza was followed by no alteration in the symptomatology or course.

Family History.—Her father died of general paresis. Her mother died in this hospital, probably from bronchopneumonia following influenza. One sister aged 19, is strong and supposedly healthy.

Past History.—She was born in Boston and spent an uneventful childhood. She graduated from the grammar school and took stenography and book keeping courses, with good records in both. She was not backward either mentally or physically and was always considered healthy until the present illness.

Present Illness.—Five years previously she was first troubled with failing vision, then with some difficulty in moving her fingers and hand (left) and was soon after taken with a complete left hemiplegia. This persisted, although the leg improved and she became able to get about somewhat, but her mother was obliged to do most things for her.

For the past two years, in addition, she has had frequent seizures in which she was unconscious for from fifteen to twenty minutes, falling to the ground, rigid, and afterward amnesic and drowsy. The seizures sometimes occurred twice or thrice a day. At other times she thought she felt quite normal. A year prior to admission she was given some intravenous injections and for five months subsequently did not faint. Three months before admission she seemed to be much better and improved in disposition.

November 27 she was taken ill with influenza. Her mother was taken ill simultaneously and died at this hospital about December 10. The patient was febrile (maximum 102 F.) for at least several days, and was in bed for over a week. She entered the Psychopathic Hospital December 6, chiefly because she was deprived of her caretaker (the mother).

She denied any change in herself since the influenza, and has not had any seizures prior to her admission to this hospital. (She had several here, however).

Mental Examination.—This was entirely negative in every way, except that the patient was somewhat restless. She seemed somewhat dull emotionally, which was thought possibly due to her recent illness. She was pleasant and fairly cheerful. She had two convulsions during her week's stay in the hospital, at which time she was unconscious, rigid, twitched, frothed at the mouth, breathed stertorously, but was not cyanosed. She took the death of her mother with considerable weeping, but reacted in a few days.

Physical Examination.—She was a rather poorly developed and badly nourished girl, 5 feet, 5 inches tall, weight, 115 pounds, with a left paraplegia. There were no marked asymmetries or anomalies. Smell, taste, hearing, vision, cutaneous and deep sensibilities were normal. There were no abnormal movements of face, tongue or lids. Coordination of the right hand was good; the left hand was paralyzed. The loss of motion in the left leg was less than in the arm. There was some atrophy of the muscles of the eye and left arm, but no vasomotor disturbance. Corneal and pharyngeal reflexes were present. The left abdominal reflex was absent. There was no Babinski nor ankle clonus. The muscles of the left side of the face were weak. All reflexes of the left side were hyperactive. The right side was normal. The left pupil was dilated and did not react. The blood pressure was 108-78. Heart, lungs and abdomen were negative.

Laboratory Findings.—The urine was negative, except for the slightest possible trace of albumin, and the presence of bile. The spinal fluid showed globulin +, albumin +, two cells. The gold sol test was 0012321100. The spinal fluid Wassermann was insufficient. The serum Wassermann was not reported.

Psychometric Examination.—The patient graded at a slightly irregular mental age of 12.5 on the point scale, and 12 years 10 months on the Stanford scale. She cooperated well.

Diagnosis.—Neurosyphilis (vascular type; congenital).

ADDENDA TO GROUP IV

Dr. Cohoon, superintendent of the Medfield State Hospital, was kind enough to make a personal investigation of the effect of the influenza epidemic on the neurosyphilitics in his institution, and has furnished his data in a personal communication. Practically all the cases there observed fall into Group 4 of this classification. Of five males, three were unchanged; two died of pneumonia. Of eleven females, two died and nine were unchanged.

This substantiates a generalization which is confirmed by all our data, namely, that the acute infection influenza has an accelerating influence on the incipient cases of neurosyphilis (and in fact on mental disease in general) which often becomes strikingly manifest, but on the advanced cases has generally no demonstrable effect, and certainly not the beneficial influence once looked for.

GROUP 5.—Cases of neurosyphilis which were apparently improved following the influenza.

We have observed no such cases, and the investigation at the Medfield State Hospital reports none. Two of the patients at the latter institution were already improving under intensified therapy, but were not perceptibly affected by the influenzal attacks. The literature mentions such cases, but in vague terms with uncertain references, so that it may safely be said that there is at present no evidence that such a fortunate occurrence ever takes place.

In the literature the example of Oeteke (quoted by Klemm[17] without reference) is typical in its vagueness. "In only one paralytic

(general paresis?) in a remission did there occur after influenza with severe pleuropneumonia a considerable and inexplicable improvement in the mental sphere."

Finally, I append two cases which are probably not cases of neurosyphilis. At least such a diagnosis cannot be made positively, although the symptoms of the one case are very typical of general paresis, and the case was so considered until the absolutely contra-indicative laboratory findings were received. When time has finally diagnosticated these cases, if it ever does, the present attitude toward them will be an interesting retrospect.

CASE 11.—*Normality (?) (+ Syphilis?) + Influenza = Mylitis Spinalis (?) Neurosyphilis.* A male, aged 37, after an attack of influenza developed urinary incontinence and sensory disturbance of the legs. The diagnosis was in doubt.

Family History.—Negative.

Past History.—Essentially negative. The patient had always been well, and he had been efficient economically.

Present Illness.—After an attack of influenza, in January, 1918, he developed a sensation of tightness over his chest and abdomen and a numbness of the legs. This began three weeks after the grippe attack terminated. Concomitantly dysuria began, followed by retention. Thereafter, he was catheterized daily and later became incontinent. At this time he was treated in an excellent general hospital. It was noted that the pupils were unequal, but reacted well, and that all reflexes were hyperactive. A lumbar puncture at this time revealed a spinal fluid containing eighty-two cells, positive globulin test, and 2 + positive Wassermann on 1 c.c. of spinal fluid. The blood Wassermann was negative. He was given two intraspinal treatments, both of diarsenolized serum with the diarsenol brand of arsphenamin reinforcements. Thereafter he received more antisyphilitic treatment and was discharged improved after three months.

He continued, however, to have the paresthesias and pains, and with them more or less difficulty with urination, which, together with his neurasthenic disposition, made him an exceedingly unpleasant companion. He was persuaded to go to the Psychopathic Hospital, where he was observed at long periods for the next year, and given considerable anti-syphilitic treatment.

Mental Examination.—This was chiefly negative, although he was exceedingly neurotic, complained much and cooperated poorly. There were no definite psychotic symptoms.

Physical Examination.—This examination showed remarkably few neurologic signs. All reflexes were hyperactive, but equal, and there were no abnormal reflexes or abnormal neurologic signs. At this time, speech and writing difficulty were thought to be present, but this was not confirmed. The blood pressure was 110-70. Some paresthesias and hyperalgesias were discovered, but nothing marked. Girdle pains were complained of at times; leg pains were also described, and vomiting attacks were sustained.

Laboratory Findings.—The twenty-four hours urine specimen was negative, except for a very slight trace of albumin. The blood cytology and blood serology were also negative. The spinal fluid examination showed globulin + +, albumin + +, nine cells, gold sol test 0001342110. The Wassermann test was negative.

Diagnosis.—A very excellent general hospital made the diagnosis of tabes dorsalis, but it was not felt here to be justifiable to retain this diagnosis. The opinion of the staff was divided on the basis of the possibilities of a modifica-

tion of the Wassermann reaction by the intraspinous treatment received. Intramedullary tumor, nonsyphilitic myelitis, and neurosyphilis spinalis were suggested as the three most likely possibilities.

CASE 12.—*Mild Premonitory Symptoms + Influenza = Pseudoparesis.* A male, aged 51, Jew, tailor, born in Russia, had resided in Massachusetts for thirty-five years.

Family History.—This was negative, except as follows: The paternal grandmother is said to have been insane for a short time (before death?); a paternal uncle "was insane in W——— state hospital. He burst a blood vessel on the brain and died after two weeks," and a paternal (female) cousin was insane for a short time after childbirth, was in T——— state hospital. "She thought she was a princess and that her mother was against her." "The paternal side are all said to be peculiar and to have an odd way of smiling at times when it was more appropriate to cry." (From wife's statement.) Siblings: The patient has two brothers in Russia, one sister in New York and one sister in Texas, "who was said to be insane for a short time."

Past History.—He came to the United States at the age of 18. He learned to read and write Hebrew at a night school in this country. He has followed various trades and invested in various businesses, including shoes, cleaning and dyeing, automobiles, tailoring and book making. He made "a comfortable living" while he owned a tailor shop, but the war conditions pushed this out of business, and since then he has been in reduced circumstances. Marital: He was married twenty-seven years previously to our chief informant, now aged 48, who was healthy and fairly happy in her married life. Children: He has a boy, aged 26, a sailor in the U. S. Navy; one boy died of grippe, aged 1 year; a daughter, aged 22, is "nervous and anemic"; a boy aged 20 is in the U. S. Army; a daughter, aged 10, is in the seventh grade. His wife has had two miscarriages, one at three months. Disposition: "He is good natured, though quick tempered, but not abusive. He is very fond of the children and helps a great deal with their care. He is active, fairly sociable, has a good deal of pride, likes to look well, and is generous." He is of the Jewish faith, but takes "no interest" (wife). Habits: He drinks beer, but never to excess. He has a good appetite.

His medical history is negative; however, "six or seven years ago he had headaches from drinking coffee and had to give it up. About seven years ago he was ill and was told by his doctor to have no sexual intercourse with his wife." This he associated with the moral of Brieux's play, "Damaged Goods," which he had just seen, and "was afraid it was something of that nature."

Present Condition.—(Where quoted, statements are taken from our historian's history as obtained from the wife.) "For about two months the patient has complained of headaches and of a noise in his ear which sounded like machinery. For about a month he has been forgetful; he would ask his wife to write down any errands he was given to do." He was laid off work on December 17, and on the nineteenth began to look melancholy. He did not complain of anything, however. The next day he went to his wife's place of employment and went to sleep, which was quite extraordinary.

December 21 he was sick in bed with influenza, his temperature reaching 100 F. The whole family had it at the same time. The next day the temperature is said to have been normal. That night, at midnight, he walked into his wife's sickroom, fully dressed, and announced that he was going to work. He looked about for some man who he said had slept there. "His temperature was taken at that time and found to be normal." He slept that night, but the next day looked "dazed and sad." He remarked, "Funny to let an audience fly," which was totally without meaning to his wife. "His body and hands shook." He went to bed but soon arose to attend to the furnace. "He staggered and appeared to lose control of his limbs. He asked for some of his children whom he should have known were away."

He began to lose weight and his breath was noted to be foul. "While in bed and apparently asleep, his eyes being shut, he talked about his work to some one he seemed to think was in bed with him." He has lost his memory for recent events, but for the remote past it remains intact. Early in the morning of December 31 he came into his wife's room, sat on the bed of one of the children, and pulled a blanket over his knees. When told to return to bed he said he was in bed and asleep. His pajamas were off and he had on a bathrobe. His wife found his own bed torn to pieces. He mumbled unintelligibly. He had had no outbursts, delusions, hallucinations (?), ideas of reference, dizziness, convulsions, shocks or fainting spells. He was admitted to this hospital January 31.

Mental Examination.—The chief findings were as follows: He was accessible and slightly cooperative. He was quite disoriented temporally, giving the day wrongly, the month as November (it was then December 31) and did not know that Christmas day, which was also his daughter's birthday, had just passed. He showed a distinct impairment of memory for recent events, but not much for remote events. He showed no frank delusions or hallucinations. His thought processes showed distinct retardation and dulling, but there was no gross incoherency or irrelevancy here shown. His emotional tone was rather flat, although there was some euphoria at times and a mild apprehension at others, when he would go about trying all the doors. His motor status was normal save for frequent exhibitions of restlessness, and periods of apparent bewilderment, described in the notes as "confusion."

Special Tests.—Speech showed a distinct defect with the conventional test phrases. His writing was also defective, and he wrote in a tremulous scrawl. The spelling is here reproduced:

181 Hann(m)mond St.
Ca?mbridges
Common w(ue)alt

Of his calculating ability the following figures made in an attempt to subtract 28 from 1918 are fully expressive:

26
168
11788
11888
1533

Ophthalmoscopic examination showed nothing abnormal in the left eye, but in the right "a dilatation of the vessels and a loss of distinctness of the nasal half of the optic disc, with evidence of mild inflammation; cup absent. Low grade monolateral optic neuritis."

Physical Examination (Summary).—Patient was a well developed and well nourished man. There were no abnormal reflexes. Local tenderness was present along the nerve trunks in the region of the right calf. The pupils were contracted, irregular, and reacted through only a moderate arc, but promptly to light. The blood pressure was 100-60 (? sphygmomometer). Coordination was good and neurologic and physical examinations were otherwise negative.

Laboratory Findings.—Blood examination: Hemoglobin, 85 per cent.; red blood count, 4,680,000 cells; white blood count, 8,400 cells. The serum Wassermann was negative; the urine was negative and throat cultures were negative. The spinal fluid showed albumin normal; globulin absent; twenty-three cells, of which thirteen were small and five large lymphcytes, and five endothelial cells. The gold sol reaction, first time showed 1112100000; the second time (same fluid) the test was negative. The Wassermann was negative.

He had a constant rectal temperature of 99.8 F. Epinephrin had no constant effect on the blood pressure. He was removed against advice by his wife who refused commitment.

CONCLUSIONS

The interrelation of coincident infections is studied from the data presented by cases of neurosyphilis affected by attacks of influenza.

Cases are cited to illustrate three effects of influenza on neurosyphilis:

1. The precipitation of profound symptoms in previously latent neurosyphilis by influenza.

2. The augmentation of symptoms and signs of neurosyphilis by influenza.

3. The absence of palpable effect of influenza on the neurosyphilitic process.

The latent, incipient, and early cases of neurosyphilis seem to be susceptible to precipitation or augmentation by the added neurotoxic effects of influenza; the advanced cases are not usually perceptibly altered in symptomatology or course.

No instances of improvement of neurosyphilis following influenza were observed.

The scanty literature is collected and epitomized.

FEVER AND THE WATER RESERVE OF THE BODY*

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INTRODUCTION

During the course of continued intravenous injections of glucose in dogs[1] and man[2] described elsewhere, fever was observed under certain conditions, namely, when the rate of sugar injection was sufficiently in excess of the tolerance limit to produce a marked glycosuria with its concomitant diuresis; when the rate of water administration was less than the rate of diuresis and when these conditions were sustained until the animal or man had lost a certain weight by dehydration. Chills were also observed to occur under the same conditions after the body temperature had begun to rise. Both chills and fever were seen to subside when enough additional water was administered. In the experiments on dogs, the rates of sugar administration were controlled by one motor driven pump, the rates of water injection by another pump. The urine was collected and measured continuously by a catheter retained in the bladder which emptied into a graduated cylinder. The animals lay constantly on the platform of a scales, sensitive to 10 grams. Under these conditions the water balance was subject to absolute control and gains or losses of 10 grams or more in body weight were readily detectable. In this way, fever and chills could be made to come and go at will during the course of a single experiment.

The most obvious explanation was that after a sufficient quantity of water had been abstracted from the body, there was not enough left to sustain the normal processes of cooling by evaporation through the lungs (and the skin in the case of man), and that the animals suffered a true thirst fever produced in an unusual way. The view was also expressed that the actual removal of water from the body might not be essential and that the mere presence of a sufficient quantity of extra

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* From the Otho S. A. Sprague Memorial Institute Laboratory for Clinical Research, Rush Medical College.

1. Woodyatt, R. T.: Studies in Intermediate Carbohydrate Metabolism. Harvey Lectures, 1915-16, p. 326.

2. Sansum, W. D.: Rapid Reduction of Intraocular Tension in Glaucoma. J. A. M. A. **68**: 1885 (June 23), 1917.

sugar in the blood and tissues might serve to bind water in a physico-chemical union which would render it unavailable for evaporation at the normal body temperature.

However, various other explanations could be formulated. It might be held that during the rapid injections of glucose an increased oxidation of sugar contributed to the end result, or that the process disturbed a nervous heat regulating "center" or that the sugar set up changes of one type or another in the cells, with fever as a secondary consequence. As a matter fact, the literature of sugar and salt fevers, beginning with Finkelstein[3] in 1908, contains discussions of all these possibilities without reaching a common decision. The literature is clear, however, in showing that sugar and salt fevers disappear when enough water is administered resembling in this respect "inanition" fever of the new-born, which as Crandell[4] showed is due to thirst. The later writers on salt fever, Heim and John[5] and Peteri,[6] clearly interpret salt fever as a result of decreased evaporation of water due to the hydropigenous (or edema producing) action of salt (sodium chlorid) in the blood and tissues. Nearly all of the literature on this subject has been contributed by the pediatricians and the fevers in question have usually followed single doses of salt or sugar by the alimentary or subcutaneous route in infants. Although fever following single intravenous injections of sugar in adults[7] had been reported before our own experiments, there was, on the other hand, enough difference between the methods of producing salt and sugar fever as described in the pediatric literature and that which we describe that at first it was not clear that we were dealing with the same phenomenon. Early failure on our part to confirm the production of fever by single subcutaneous, alimentary or intravenous administrations of sugar in adult dogs or man, suggested that we were not. But it was later found that this could be done consistently in dogs if the animals were made sufficiently thirsty beforehand. The uniform success of certain pediatricians in producing salt fever in babies suggests that they also have worked regularly with thirsty animals.

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3. Finkelstein, H.: Ueber Alimentäre Intoxikation. Jahrb. f. Kinderh. **68**: 693 (Dec.), 1908.

4. Crandell, F.: Inanition Fever. Arch. Pediat. **16**: 174 (March), 1899.

5. Heim, P. and John K.: Pyrogene und hydropygene Eigenschaften der Physiologischen Salzlösung. Die Bedeutung und Behandlung Exsiccation. Arch. f. Kinderh. **54**: 65, 1910.

6. Peteri, I.: Beiträge zum Pathologischen Wesen und zur Therapie des Transitorischen Fiebers bei Neugebornen. Jahr. f. Kinderh. **80**: 612 (Dec.), 1914.

7. Bingel, A.: Ueber Salz- und Zucker-Fieber. Arch. f. exper. Path. u. Pharmakol. **64**: 1, 1910.

Our own experiments appeared to offer a very good method of producing and allaying fever in the laboratory under conditions more susceptible to control than any method heretofore used, and it was thought advisable to test its limits as a method. The experiments herein described were undertaken primarily for that purpose. It was also thought desirable to employ the method to investigate further into the mechanism of this type of fever and chills in the hope that light might be thrown on the mechanism and possibly the rational management of fevers and chills in general, particularly the toxic fevers, such as typhoid, the mechanism of which has not yet been settled. Several points bearing on these questions are elaborated in the discussion. The question presents itself as to whether all ordinary clinical fevers are not due in the last analysis to a deficit of free water in the body.

EXPERIMENTS

These were designed to determine:

1. How high the temperature of the body can be driven by the technic in question.

2. Whether or not an increased combustion of glucose is a contributing factor.

3. Whether the fever is due to a primary effect of the sugar on the water of the body or whether it is secondary and dependent in any way on a nervous "center" or nervous heat regulating mechanism.

4. Whether it is necessary actually to remove water from the body or whether molecules of sugar within the body can produce fever by their mere presence.

The experiments show that the body temperature can be driven to remarkable heights by this method. Fevers of 111 F. are readily produced, and in one case the body temperature rose to 125.6 F. Fevers of 111 F. were produced by means of salt (NaCl) and by lactose, showing that the increased combustion of glucose is not a necessary factor, which was the conclusion to be anticipated in view of the fact that diminished heat loss and not increased heat production (or supply) is known to be the determining factor in all fevers, that is to say, a great increase of heat production alone does not cause fever because normally a great excess of heat is disposed of automatically by increased cooling. The experiments show that sugar is capable of causing fever by its mere presence in the body under certain circumstances, but that no quantity of sugar which can easily be introduced will cause fever unless the water reserve of the body is for some reason sufficiently low to begin with. Finally, sugar fever can be

produced in dogs which have been rendered poikilothermic by severing the cervical cord, and therefore these fevers are in no sense dependent on a nervous heat regulating mechanism.

EXPERIMENT 1.—A female bull-terrier, weighing 9.3 kilos, was injected intravenously, with a 36 per cent. glucose solution, at the rate of 15 gms. of glucose per kilogram of body weight per hour, for a period of ninety minutes. During this time the animal received 614 c.c. of the glucose solution (containing 221 gms. of glucose) and passed 1,230 c.c. of urine, containing 68.4 gms. of glucose; a retention of 152.6 gms. The fluid output exceeded the intake by 616 c.c., or 66.2 c.c. per kilo. The temperature (vaginal), which was 102 F. at the beginning of the experiment, increased to 102.5 F. by the end of the first hour. A severe chill began twenty-one minutes later and the dog was covered with a woolen blanket. Nine minutes later violent convulsions began and the temperature was found to be 111.2 F. The convulsions became so violent that it was necessary to stop the injection. The urine ceased to flow and thirteen minutes later the dog died with a temperature of 125.6 F., the highest animal temperature that we have been able to find on record. The rise of temperature after the cessation of diuresis amounted to 14.4 degrees.

A postmortem examination was made immediately after death in the presence of Prof. H. G. Wells. The blood was turbid. The red blood cells were crenated to a marked degree. The heart was uniformly dilated to the limit of the pericardial sac. The kidneys and liver were in a state of "cloudy swelling." (Note that in spite of the loss of 66.2 c.c. of water for each kilogram of body weight, with crenation of the red cells, the parenchymas of the liver and kidneys, though dry to the touch, had the appearance of "cloudy swelling.")

EXPERIMENT 2.—The course of this experiment was similar to that of the above, except that no covering was thrown over the animal at the onset of the chills and the diuresis and temperature rise were not so marked.

The dog, weighing 16.9 kilogram, received a 36 per cent. glucose solution, at the rate of 15 gm. per kilogram per hour, for ninety minutes. During this time the fluid intake was 1,029 c.c. and the urinary output 1,470 c.c., a dehydration of 441 c.c. or 27.8 c.c. per kilogram. The temperature, which was 100.4 F. at the beginning of the experiment, rose to 109.4 F.

2.78%

In previous experiments with glucose injections at the rate of 3.6 gm. per kilogram per hour it was shown that only about 0.6 gm. per kilogram is actually burned. However, the amount of combustion might increase somewhat with the higher rate of injection. Accordingly, increased combustion of glucose might be advanced as an explanation of the abnormally high temperature. We have never been able to give glucose at the rate of 15 gm. per kilogram per hour and maintain the water balance, because the heart is not capable of propelling the necessary volume of fluid. Consequently, we have not been able to determine the rate at which glucose actually burns under these conditions. But we have given 10 gm. per kilogram per hour for a period of seven hours, maintaining the water balance, without the advent of a rise of temperature. (The injection of glucose at rates above 2 gm. per kilogram per hour, will be discussed in a paper on "Intravenous Injections of Glucose at Higher Rates," now being prepared.)

We also performed two experiments, dehydrating with hypertonic sodium chlorid-sodium carbonate solutions, to ascertain how high a temperature might be obtained by employing crystalloids which do not burn in the body.

EXPERIMENT 3.—A female bull-terrier, weighing 10.4 kilograms, was given intravenously 753 c.c. of a 1.4 per cent. sodium chlorid—1 per cent. sodium carbonate solution, over a period of three hours. During this period the dog passed only 255 c.c. of urine. There was, therefore, no absolute dehydration. The temperature, which was 102.2 F. per vagina at the beginning, did not change. The concentration of sodium chlorid was therefore raised to 5 per cent. During the next two hours and thirty-five minutes the dog received 800 c.c. of this new solution and passed 1,875 c.c. of urine. During the course of the five hours and thirty-five minutes of the total injection, the dog received 1,553 c.c. of fluid and passed 2,130 c.c. of urine, a net output over intake of 577 c.c. or 55.5 c.c. per kilogram. Convulsions began and the injection was stopped thirty minutes before death. The temperature rose from 102.2 F. to 113 F. A rise of 9 degrees occurred after the cessation of urinary flow.

Excessive muscular activity during the convulsions might be suggested as a cause of the high temperature. To eliminate this factor a similar experiment was planned and the animal fully narcotized with ether at the first signs of chill, thus preventing the advent of convulsions.

EXPERIMENT 4.—A dog, weighing 10.4 kilograms, received, for a period of three hours, 718 c.c. of a 5 per cent. sodium chlorid—1 per cent sodium carbonate solution, and passed 1,005 c.c. of urine. The fluid output exceeded the intake by 287 c.c. or 28.2 c.c. per kilogram. The first slight twitchings due to a beginning chill began thirty-eight minutes before the close and were immediately stopped by the anesthetic. The temperature rose from 101.3 F. to 111.2 F.

Fever in Poikilothermic Dogs.—In order to determine whether the temperature changes during these experiments were in any way grossly influenced by a nervous mechanism, several dogs were rendered poikilothermic by sectioning their spinal cords between the sixth and seventh cervical segments. These dogs were also observed for manifestations of chills. Several experiments were made before the results were satisfactory. Following section of the cord, the body temperature adjusts itself to that of the environment and, at ordinary room temperature, it falls steadily and only becomes constant again at a deeply subnormal level. Under such conditions glucose injections may fail to start diuresis. If diuresis does occur, and it is possible to dehydrate in the usual way, the body temperature may rise materially and still the final temperature may remain markedly subnormal so that one could not then speak of having produced fever in the absolute sense. Again, if the attempt is made to keep the body temperature from falling too low by means of heating appliances, there is danger that fever may be pro-

duced accidentally by the external heat, and it requires elaborate equipment to maintain an operating room constantly at the desired temperature. The simplest method, and one that proved entirely practical, was simply to swathe the animal in cotton or blankets immediately after the operation. In this way the temperature may be kept constant for hours at a level only slightly below the normal.

EXPERIMENT 5.—The spinal cord was sectioned as described above. During the next four hours the dog cooled, spontaneously, to 83.3 F. It was then taken to a room heated approximately to this temperature, 84.4 F. During the next three hours, the dog, weighing 11.5 kilograms, received intravenously 582 c.c. of a 70 per cent. glucose solution, and passed 765 c.c. of urine. The fluid output exceeded the intake by 183 c.c. or 15.9 c.c. per kilogram. The temperature rose from 83.3 F. to 93.2 F., a rise of 9.9 degrees. Slight twitchings of the muscles of the neck and face began just before the death of the animal. Otherwise the usual outward manifestations of chill were missing.

EXPERIMENT 6.—An attempt at dehydration, in an animal whose temperature had been allowed to fall to 77 F., failed on account of the lack of diuresis. An increase in temperature of only 1.8 degree was noted.

EXPERRIMENT 7.—In this experiment the cord was severed as before. A covering was placed over the animal to prevent too great loss of heat. In the course of three and one-half hours from the time of the operation, the temperature gradually fell to 95 F., where it remained constant for four hours. During the next four hours the dog received intravenously 752 c.c. of a 61 per cent. glucose solution and passed 1,640 c.c. of urine. The fluid output exceeded the fluid intake by 888 c.c. or 71 c.c. per kilogram. The temperature rose from 95 F. to 106.7 F., an increase of 11.7 degrees. There were no external manifestations of chill and no convulsions.

These experiments prove that the fevers in question are not dependant on a nervous mechanism.

DISCUSSION

General Principles.—Because of its high specific heat, water is capable of absorbing large quantities of heat, thus preventing sudden high temperature rises in the cells.[8, 9, 10, 11] (It is a noteworthy fact that those tissues in which most heat is produced contain the highest percentage of body water.) Having absorbed heat from its sources of production, water, because of its fluid nature, is capable of distributing the heat equally throughout the body and carrying the excess to the surface where it may be given off. Water then acts as a buffer in high temperature changes, and as a vehicle of heat within the animal body.

8. Mathews, A. P.: Textbook of Physiological Chemistry, New York, 1916.
9. Henderson, L.: The Fitness of the Environment, New York, 1910, p. 80.
10. Stewart, G. N.: Manual of Physiology, New York, 1914.
11. Hunt, E. H.: Regulation of Body Temperature in Extremes of Dry Heat. J. Hygiene **12**: 479, 1912.

Rubner,[12] Wolpert[13] and Zuntz[14] have established that, in a normal body, as heat production increases, heat elimination by radiation, conduction and evaporation also increase, but that the percentage of heat dissipation by evaporation continually increases as more heat is produced. In other words, normally the loss of heat through evaporation fully compensates for that which cannot take place through radiation and conduction in order to preserve the normal temperature. In fever, however, this is not true. Krehl and Matthes[15] found that during fever, although there was usually an increase of heat elimination by radiation and conduction as well as by evaporation, the loss by evaporation was not sufficient to maintain a temperature equilibrium as in a healthy body. This failure of evaporation to compensate for the loss of heat which cannot take place through radiation and conduction would indicate that something hinders the evaporation of water in fever. Either the total supply of water runs out or the water becomes more firmly bound in the tissues and less available for evaporation.

Further investigations show that when the compensatory loss of heat by evaporation is hindered, hyperthermia results. This has been demonstrated by Sutton[16] who subjected human beings to high temperatures in an atmosphere which contained enough moisture to prevent evaporation. Similar results were observed by Haldane[17] in miners working in warm, damp mines. That most fevers are caused by increased atmospheric temperature, and moisture is of course out of the question. This is true only in cases of sunstroke, heat prostration or the like.

How then may evaporation of body water be checked in other ways? One method of accomplishing this purpose lies in the actual removal of water from the body to the extent that not enough remains to carry off the excess heat. Theoretically, if all the water should be removed from the body the specific heat of all the tissues would be reduced, and with no means left of quickly conveying it to the surface heat would accumulate in the tissues of the body and a high pyrexia

12. Rubner, M.: Die Beziehungen der Atmosphärischen Feuchtigkeit zur Wasserdampfabgabe. Arch. f. Hyg., 1890.

13. Wolpert, H.: Ueber den Einfluss der Lufttemperatur auf die im Zustand anstrengenden Körperlicher Arbeit ausgescheidenen mengen Kohlensaure und Wasserdampf beim Menschen. Arch. f. Hyg. **26**: 32, 1896.

14. Zuntz, N.: Ueber die Wärme Regulierung bei Muskelarbeit. Berl. klin. Wchnschr. **33**: 709 (Aug.), 1896.

15. Krehl, L. and Matthes, M.: Wie entsteht die Temperatursteigerung des fiebernden Organismus. Arch. exper. Path. u. Pharmakol. **38**: 284, 1896.

16. Sutton, H.: The Influence of High Temperature on the Human Body, Especially with regard to Heat Stroke. Path. and Bacteriol. **13**:62, 1908.

17. Haldane, J. S.: The Influence of High Air Temperature. J. Hygiene **5**: 494, 1905.

would result. This, of course, practically is an impossibility, for a certain amount of water must be present in order that chemical reactions may take place, but less extreme water deprivations, as confirmed by clinical and experimental evidence, inevitably lead to hyperthermias of various degrees.

The researches of Hunt[11] on the effects of prolonged perspiration indicate that there is a large reserve of water in the body tissues which is called out in emergency. Though a large amount of water may be lost without any change in temperature, this investigator believed as a result of his work, that exhaustion of the reserve water would have the same effect as prevention of evaporation by increased atmospheric moisture. So far as we are aware, he did not subject this view to direct experimental test. The present experiments do exactly this thing, and the results are in complete harmony with Hunt's conception.

Sugar Fever; Salt Fever.—This brings us to the discussion of sugar and salt fevers as described by the pediatricians. In 1899, Floyd Crandell[4] in an article on inanition fever credits McLane of New York with having first described the phenomenon of fever which develops in the new-born prior to the establishment of the regular flow of breast milk and subsides thereafter. McLane called it inanition fever, believing that the solids of the milk were what allayed it, but Crandell showed that water alone was equally effective, and that the condition was not due to inanition, but to thirst. Similar observations were made by Erich Mueller[18] concerning a form of fever which Halberstadt saw in infants undergoing changes of diet. In 1906, Schaps[19] reported that subcutaneous injections of small quantities of isotonic sugar or salt solution caused fever in normal infants reaching a crest in 8 to 10 hours to disappear within 24 hours. He reported that repetitions of the dose gave weaker results.

We have not seen anything comparable to what Schaps describes and mention it merely in passing as a type of sugar or salt fever which, if it occurs at all, is something different from that which we are here discussing,[20] but in 1908-9 Finkelstein[3] described fever after feedings of 100 c.c. of 12.5 per cent. lactose solution to infants with intestinal disorders. Other sugars and also salts produced the same results. Finkelstein's solutions were strongly hypertonic, his doses were large and his results have been amply confirmed. He made the

18. Mueller, E.: Durstfieber bei Saüglingen. Berl. klin. Wchnschr. **47**: 673, 1910.

19. Schaps, L.: Salz und Zucker Injektion beim Saügling. Gesellsch. f. Kinderh. **23**: 153, 1906.

20. The febrile reactions observed by Schaps and others with isotonic salt solutions have since come to be considered as due to the use of water which was not freshly distilled.

observation most significant in the present discussion, that these fevers could be made to disappear entirely by the administration of tea and even water alone. Thus, Finkelstein saw another kind of fever in infants which, like those described by McLane and Halberstadt, yield under water administration. However, Finkelstein was not clear as to the mechanism of his sugar and salt fevers, and ventured the opinion that they arose from "injuries to cells" caused by the physico-chemical effects of the sugar or salt. Finkelstein thought the cells were injured by physicochemical effects of the sugar or salt rather than by chemical effects, and that much is important. Following Finkelstein a number of communications on the same subject appeared which confirmed the facts but confused more than they clarified the question of mechanism, except the writings of Heim and John,[5] and of Peteri.[6] In summing up the literature in the light of his own observation, Peteri, in 1914, concluded that infection played no part, that external conditions of the atmosphere had been excluded, that the immediate causative factor is desiccation and that the height of the fever attained is in inverse ratio to the body weight. All of these conclusions are in perfect accord with our own reading of the literature, and the results of the present experiments bring proof of their correctness.

Heim and John concurred with Finkelstein's observation that sugars and salts operate to produce fever by their physicochemical effects, which is obvious, for when fever is produced by intravenous injections of lactose, every gram of the lactose given is recoverable unchanged in the urine. The lactose molecule has not been altered. It has done its work as a molecule. But Heim and John went further. Instead of saying that the sugar or salt acted in some unknown physicochemical way on the cells causing the cells in some other unknown way to produce fever, thus begging the question, they suggested that the molecule (of salt) enters the cell and increases the affinity of the cell for water and that it does it in this way. Salt molecules have an affinity for water, and if several hundred of them migrate into a cell, the cell containing them becomes endowed with an increased affinity for water just because it has more salt in it.

This is the conception which Hofmeister first expressed in explanation of the power of a salt in suitable concentration to increase the swelling of colloid jellies. Thus salt in the body holds water in the body by its "hydropigenous" (or edema producing) tendency. As a result, the elimination of water through the lungs and skin falls, cooling is retarded and the body becomes overheated by the continuance of its own metabolic fires. And, it may be added, that as the body warms up more and more, the metabolism becomes faster and faster; a vicious circle is established.

It is unnecessary in this place to delve further into the nature of the affinity of molecules of salt or sugar for water, or to discuss theories of the character of the physico chemical unions of salts or sugars and water in general. It is enough that salts and sugars generally do tend to hold water in association with themselves, and that these substances when added to a beaker of water increase its boiling point and retard its evaporation at any given temperature and pressure. The same may occur in the body. As previously pointed out, the work of the pediatricians with salt fever has been conducted on infants which were in all probability considerably dehydrated to begin with, for as Peteri noted, the heights of the fevers resulting from sugar or salt administrations appear to be related in inverse ratio to the body weight, while fluctuations of body weight are determinated largely by the water balance. Moreover, water stops the fever. Our own experiments demonstrate sharply that single large injections of sugar do not, as a rule, cause fever unless the animal is first depleted in water. Therefore, it seems clear that Hunt is right — that there is normally a reserve of water in the body; that a certain fraction of this may become bound by sugars or salts added to the body, but that this binding of water will not ordinarily exhaust the whole free water reserve and determine fever unless the water reserve has been depleted beforehand by actual removal of water from the body as by continued elimination through the lungs, skin, urine or bowels without replacement.

We believe that the discussion up to this point shows that "inanition" fever of infants, the fever seen by Halberstadt in infants during alterations of diet, sugar and salt fever in infants, in adults and in animals, are all thirst fevers due to a retarded evaporation of water caused by exhaustion of the body reserve of water available for evaporation at the normal body temperature. One cannot help asking the question: How many more of the fevers which we know in the clinic can also be drawn into the same category?

A PHYSICOCHEMICAL THEORY OF FEVER

We have entertained the following proposition:

Fever, *the symptom* as seen in typhoid, malaria, pneumonia, tuberculosis, rheumatism, measles, serum reactions, proteose intoxication and all ordinary febrile diseases, except insolation and the like, may mean a deficit of "free" water in the body. By the term "free" water we would convey the idea of water in states comparable to those of liquid water at from 20 to 40 C. and ordinary pressures. As A. P. Mathews points out in his book on Physiological Chemistry, 1915, pp. 190-191, the works of Eötvös, Ramsay and Shields and Armstrong, show that

in liquid water at from 20 to 40 C. there probably exist several kinds of molecules ranging in formula from $(H_2O)_2$ to $(H_2O)_4$. But in any case, in the present connection "free" water is used to suggest liquid water, capable of absorbing excess heat from the cells, conveying it via the blood to the surfaces of the body and there dissipating it by evaporation, all at the normal body temperature.

Over against "free" water the body contains "bound" water. By this term is meant water molecules associated in the form of hydrates with molecules of other substances such as salts, sugar, protein, etc.; also, of course, water in true chemical combination, but especially the hydration water in colloids. This would correspond to the water reserve of Hunt. It is assumed that the "free" water tends to be in equilibrium with the "bound" water, and that there is a tendency toward the maintenance of a certain "free" water concentration in the blood more or less analogous to the hydrogen ion concentration of the blood, or the blood sugar concentration. When a certain quantity of "free" water is eliminated from the body, its place is filled by more water liberated from the hydrate reserves, and when an excess of free water is taken into the body it is stored as hydrate water or eliminated from the body.

As the colloids are extremely sensitive and prone to change in their capacity to hold water in response to the subtlest chemical and physicochemical influences, it is easy to conceive how the maintenance of a uniform "free" water concentration in the blood might be susceptible to a certain degree of vasomotor nervous control. Thus, the vasomotor nerves, by constricting blood vessels in the liver and causing a relative asphyxia in the liver may increase the production of acid in that organ and so liberate more free glucose from its storage form — glycogen. In an analogous way vasomotor nerves might cause colloids to take up or release more water by causing changes of cell metabolism through variations in the blood supply as needs arose. But the same thing could be accomplished directly by physicochemical and chemical agencies without the assistance of nerves, and nerves could not regulate temperature unless there were free water and responsive cells for the nerves to influence.[21]

It is proposed that in the ordinary febrile diseases, such as typhoid, tuberculosis and others, the symptom fever is due to a deficit of "free" water resulting from an abnormal tendency on the part of the colloids of the body to bind water. The poison of the disease leads to changes of the cell colloids and increases their hydration capacities, so that they

21. The reader will note that we are discussing fever and the means of the body to prevent hyperthermia or excess of heat; we are not discussing other phases of the problem of regulation of the body temperature.

tend to take up and bind more water. The effect of this on the "free" water of the body is thus the same as that of thirst or the introduction of salt or sugar into the body from without.

It would follow from the above that if we measured the "free" water of the blood in fever, it would be found low even if the total water content of the body were high. It is known that the blood as a whole does commonly become concentrated in fever, but as yet we have no ready method of measuring the "free" water fraction, although means by which this might be accomplished suggest themselves. It would also follow that the cells should be found swollen, the secretions concentrated, etc., which, of course, is the general rule in fever (cloudy swelling of the parenchymatous organs). The thirst during fever and the sudden release of water in the form of urine and perspiration when fever ends by crisis point directly to an abnormal binding of water during the period of elevated temperature. Everyone is familiar with the remarkable emptying out of water via the kidneys and skin which may follow the crisis in a case of pneumonia. Liters of water may thus be liberated in a few hours, giving visible proof of the water retention of the febrile stage. Finally it would follow that if enough water were introduced into the body during fever to saturate the increased affinities of the colloids and provide an excess of free water, then fever should disappear entirely. Now it is possible by copious water administration to lower high grade fevers and to make low grade fevers disappear. The value of plenty of water in fever, and especially in the management of tuberculosis, is too well recognized to require discussion, but probably no one has yet daringly pushed the administration of water in fever to the ultimate limits which might be necessary to ascertain whether every fever can be made to disappear entirely if enough water is given.

The question as to whether it would be good for every patient who presents the symptom fever to eliminate this symptom by means of copious water administration if that were possible, is a question that has been raised repeatedly by friends to whom the present views have been presented. We may be pardoned, therefore, if we emphasize the fact that this question is not under discussion in the present paper. The first objective is to determine whether the symptom fever can or cannot be controlled in this way in a large percentage of cases, and the wisdom of doing so if possible would then remain to be determined by sufficiently numerous experiments in various special types of cases. It is quite conceivable that in some cases the tissues might be so badly poisoned that they would partially liquefy if sufficient water were supplied, and still leave no "free" water available for evaporation at 37 C. The administration of water might then be pushed until mas-

sive edemas or general anasarca supervened before a reserve of free water could be established, or it might prove impracticable to accomplish the desired result at all. These are questions to be answered by experiments.

Up to the present time we have conducted three experiments in pneumonia patients in all of which the body temperature returned to normal within twenty-four hours with the administration of eight liters or less of water. Several observations on diphtheria cases were indecisive, fever persisting in one case after the administration of ten liters of water. A dog poisoned with diphtheria toxin, on the other hand, ran a persistent temperature between 104 and 105 F., until given a large intravenous injection of 3 per cent. glucose solution, during which the temperature fell to normal within five hours. Other work is in progress. So far the results are considered as indecisive.

In closing, attention is invited to the recent work of Lillian Moore,[22] who repeats the experiments which have formed the entire basis for the conception that there are nervous "heat centers" in the brain which, when stimulated, may cause fever.[23] Her results were negative and she draws attention to the absence of any sound experimental support for the current teaching that ordinary fevers are due to derangements of any demonstrable nervous mechanism. She points to the need for a physicochemical theory of fever. The theory outlined above may, therefore, serve to fill a gap. It has at least the advantage that all of the factors which enter into it are concrete things that may be subjected to measurements, and it should be capable of sharp proof or disproof by well designed experiments without recourse to opinion. Whatever the outcome of such experiments, they will, perhaps, add something to our knowledge of the problem.

22. Moore, Lillian: Normal Temperature Variations and the Temperature Effects of Operative Procedures. Am. J. Physiol. **60**:24, 1918. Relation of the Corpus Striatum to the Regulation of Body Temperature. Am. J. Physiol. **46**: 253, 1918.

23. The Regulation of body Temperature. Ed. J. A. M. A. **71**:1139 (Oct.), 1918.

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